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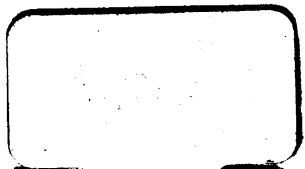
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COMPRISING TEN VOLUMES ON THE YEAR'S PROGRESS
IN MEDICINE AND SURGERY

UNDER THE GENERAL EDITORIAL CHARGE OF
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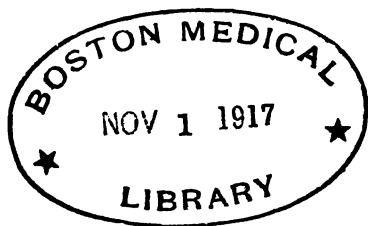
VOLUME VI GENERAL MEDICINE

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GENERAL MEDICINE.

PUBLISHER'S NOTE.

Owing to the absence of Dr. Billings in Russia the final revision of the manuscript for this volume was left in charge of the assistant editor, Dr. Raulston, and the general editor of the series, Dr. C. L. Mix.

INFECTIOUS DISEASES.

GENERAL CONSIDERATIONS.

Non-Specific Substances in Infectious Diseases. The therapeutic measures used in the treatment of infections are divided by James W. Jobling¹ of Nashville, Tenn., into two general classes: First, those specific substances which are supposed to destroy the infecting organisms or neutralize its toxins, and second, those which aim to strengthen the natural processes that normally bring about recovery.

He says that the work done in most of the experiments made to find curative agents for the various infections has evidently been based on the assumption that a substance must be found which will act directly on the infecting organism, or that will cause a mobilization of those specific immune bodies which we are accustomed to look on as Nature's agents in bringing about recovery. And yet, one finds a considerable accumulation of evidence, both from the laboratory and from the clinic, which definitely indicates that certain non-specific and as yet, ill-defined factors have a large share in bringing about recovery from disease. While the emphasis placed on certain phases of immunology and specificity, more especially the fruitful antigen-

(1) Archiv. Int. Med., June, 1917.

antibody conception of Ehrlich, has been of inestimable value. Jobling is inclined to believe that it has resulted in the neglect of certain perfectly obvious lines of approach to medical problems.

That specific vaccines are effective in the treatment of acute general infections is shown by numerous reports, dating back to Frankel's work in 1893 and covering the field of medical advancement up to the present. While these results may not have been entirely uniform in character, sufficient evidence is afforded to show that the older ideas concerning the principles on which vaccine therapy were based do not afford a satisfactory explanation.

Matthes is quoted as having demonstrated early in the development of tuberculin therapy that to all intents and purposes the reaction considered specific for tuberculin could be produced with deuto-albumose, and he showed that whatever difference did occur could be explained by the fact that the tuberculin fraction contained certain toxic peptones in addition. Matthes, later, went even further, expressing the idea that fever in general was produced by protein split-products, and he suggested the importance of proteolytic ferments in this connection, thus foreshadowing the work of Vaughan in this country, and the later German workers who dealt with the phenomenon of anaphylaxis.

Immediately after Frankel treated typhoid fever to advantage with vaccines in 1893, Rumpf obtained a similar favorable result with vaccine composed of the *Bacillus pyocyaneus*.

In America, too, the controversy occasioned by the Schäfer vaccine is pertinent. The fact that the Schäfer vaccines were palpably non-specific was sufficient, Jobling says, to warrant the stamp of disapproval by the medical profession.

The effect of non-specific substances has been demonstrated by the dermatologists within the past three years in a variety of diseases, including some cases of psoriasis which have proved refractory to other methods of treatment. Recently, Engman and McGarry have reported favorable results in treatment of lupus erythematosus with intravenous injections of typhoid bacilli.

Ichikawa, who was among the first to use the intravenous method of administering vaccine in typhoid fever, observed that the results in paratyphoid patients who had been treated with typhoid vaccine were similar in every way to those noted in typhoid fever. Kraus obtained a similar result in the treatment of typhoid fever with the intravenous injection of vaccines of colon bacilli.

Hiss and Zinsser used extracts of rabbit leukocytes in the treatment of epidemic cerebrospinal meningitis, pneumonia and staphylococcus infections, and believed that the course of these diseases was favorably influenced.

Miller and Lusk treated a series of patients with typhoid fever by intravenous injections of typhoid bacilli, and also secondary proteoses. In this series 20 per cent. terminated by crisis and 20 per cent. by rapid lysis. They also treated a series of chronic, subacute and acute cases of arthritis with these preparations, with excellent results, as relief was afforded in the majority of cases. The authors do not state the number of patients treated by each method, but conclude that both give the same results.

A series of gonorrheal complications, especially arthritis, epididymitis, and acute prostatitis, in which the patients were treated with a variety of vaccines composed of gonococci, meningococci, colon bacilli and with secondary proteoses, has been reported by Culver. Twenty-eight of the thirty-one arthritic patients were either completely cured or manifested a decided improvement. The twelve patients with acute epididymitis presented complete freedom from pain after the first injection.

Manier, Peterson and Jobling treated thirteen cases of arthritis, with secondary proteoses. Seven of these patients suffered from chronic, and six from acute arthritis. All of the acute conditions were apparently cured, all of the chronic greatly helped, except in one instance, and three of the patients with chronic arthritis were apparently cured. Four patients with gonorrheal epididymitis with acute swelling and tenderness of the epididymis were treated; in every instance there was immediate improvement following the first injection, the

epididymis becoming smaller and distinctly less tender. Two patients with erysipelas were treated and apparently entirely cured.

Jobling states that the purpose has been to obtain some increase in temperature with a slight chill, and this reaction was usually obtained at the first injection with 0.25 c.c. of a 1 per cent. solution. Injections were given, in most instances, every day, as some patients required but one and others as high as eighteen injections. As the reaction varies in different individuals, he thinks it better to begin with the smaller dose and thus establish the tolerance of each patient before pushing the treatment. In no instance were there any alarming symptoms.

In describing the reaction obtained, Jobling says that immediately following an injection by this method of treatment, there is usually a reaction which is sometimes severe. As a rule there is a chill from one-half to one hour following the injection, and this may last from 15 to 45 minutes. With a chill there is an increase in temperature of from 1 to 4 degrees F., followed several hours later by a progressive fall. Associated with the drop in temperature, there is general relaxation, profuse perspiration and a rapid subjective and objective improvement. The pulse may or may not be increased in frequency. Following the injections the leukocytes are decreased in number, sometimes as low as 2,000 per cubic millimeter. This leukopenia is followed by a gradually developing leukocytosis, but usually reaches its maximum in from five to seven hours.

Immediately following the injections—in acute infections, such as typhoid fever—there may be a permanent return to the normal temperature—there is termination by crisis; the temperature and general condition may improve more slowly—termination by lysis; or all the symptoms may return and the disease progress as usual, uninfluenced in any manner, though usually it pursues a milder course.

Hemorrhage is the most serious complication that has been reported in the treatment of typhoid fever by this method. Ichikawa has observed this and believes that previous hemorrhages contraindicate this form of treat-

ment. Some have considered organic heart disease, pregnancy, and hypertension as contraindications also.

Concerning the mechanism by which this treatment produces good effects, Jobling says that it is now the general belief that the hematopoietic organs are the chief source of antibodies and not the tissue cells in general. As a corollary of this idea concerning the source of antibodies, it would be reasonable to suppose that any disturbance of the hematopoietic system might alter the antibody formation. In view of these facts it is possible that the various agents may act as stimulants of the hematopoietic tissue, thus suddenly flooding the body with immune substances, and thereby overcoming the infection.

It is said that observations appear to show that the mobilization of antibodies must play a minor rôle in recovery from infection following the use of non-specific substances.

It is a common clinical experience that in some diseases, among them subacute joint diseases, neuralgia, diabetes, pernicious anemia, certain dermatoses, sarcoma, etc., distinct beneficial results follow at times on some intercurrent febrile condition. May it not be, then, that these non-specific substances influence the course of the disease by producing a high temperature?

The disappearance of acute gonorrheal infections coincident with chills in malaria, as reported by Culver, bears directly upon this point.

The importance of the leukocytic reaction has been emphasized by various authors, but it has been seen that in considering the part leukocytosis may play in the recovery from disease we must consider other factors in addition to phagocytosis. Peterson and Jobling have already pointed out that in experimental animals intravenous injection of bacteria, kaolin, protein split-products and trypsin is almost invariably followed by more or less marked mobilization of serum proteose and usually of esterase. Similar reactions occur in patients following the intravenous injections of vaccines and proteoses, but not to the same degree nor with the same regularity as in animals.

There remains some question as to the final value of

this mobilization of ferments. Concerning antiferment, the immediate effect of the vaccine and proteose injection is not an increase, but a distinct decrease, in the antiferment titre for a short period of time, followed later by a rise. The exact cause of these changes in the antiferment index remains undetermined.

Jobling and his co-workers have also found that there are distinct changes in the viscosity of the serum of animals undergoing immunization, and that similar changes occur in anaphylactic shock. This alteration of serum may be of more than theoretical interest in the interpretation of results obtained by the intravenous injection of non-specific substances. These changes are always, more or less, temporary in character and will therefore not explain the permanent recovery of patients treated in the early stages of such diseases as typhoid fever.

In conclusion, the author states that according to present views the symptoms of an infection are the result of the struggle between the infecting bacteria and their toxins, and the protective agencies of the host. Theoretically, then, the results observed might be due either to the destruction of the infectious agent with its products, or to the fact that the cells of the host become resistant to the action of these agents. In either case, from the present point of view the disease ceases to exist. Theobald Smith, in 1910, said: "The effectiveness of vaccines applied in the course of acute febrile diseases, such as typhoid and pneumonia, must be accounted for by principles of which experimental medicine has as yet no definite knowledge," and this view apparently holds true at present.

That the intravenous injection of non-specific substances exerts a marked influence on those infections in which it has been tried is very evident, Jobling says. Of course, these newer methods will not cure all cases of infections. They do, however, open up new possibilities and suggest new methods for attacking infections of unknown etiology, as also those caused by organisms for which we have no specific antisera. That all cases are not benefited does not necessarily reflect on the value of the treatment. There are very few

therapeutic measures which do not have the same objection.

The Intravenous Use of Foreign Proteins in Infectious Diseases. Working in the medical clinic of Joseph L. Miller at Cook County Hospital, Francis J. Scully² has used foreign protein intravenously in various pathologic conditions. The protein employed was typhoid bacilli, killed by heating to 70 degrees C. for two hours. The suspension was so made that each cubic centimeter contained 150,000,000 bacteria and injections of from 0.25 to 0.5 c.c. were used as the average dose.

From half an hour to an hour following the injections

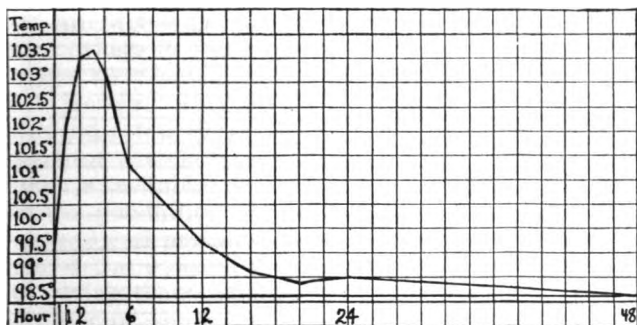


Fig. 1.—Composite temperature curve following forty-seven intravenous injections of typhoid vaccine in twenty-five cases of acute articular rheumatism.

there were no apparent changes in the patient's condition, then a chill occurred, which might become quite severe and was accompanied with the usual symptoms of cyanosis and rapid pulse. With the onset of the chill the patient usually complained of a dull temporal headache; nausea and even vomiting were frequent at this time. The chill lasts from fifteen to thirty minutes and subsides gradually, the headache and nausea passing away with it. There seems to be a profound vasomotor disturbance, which may account for the sudden deaths that have been reported following intravenous vaccines.

In some instances when the reaction was severe, there were noted, also, herpes about the lips, headache and

(2) Jour. Amer. Med. Ass'n., July 7, 1917.

vomiting. The accompanying chart (Fig. 1) shows a composite curve of forty-seven injections in twenty-five cases of acute articular rheumatism, and may be taken as a typical temperature curve.

A chart of the variation in the numbers of leukocytes (Fig. 2) contains a curve representing an average of forty-three injections in twenty-four cases, and may be taken as a typical leukocytic curve. Following the injection, and especially at the time of the chill, there was a

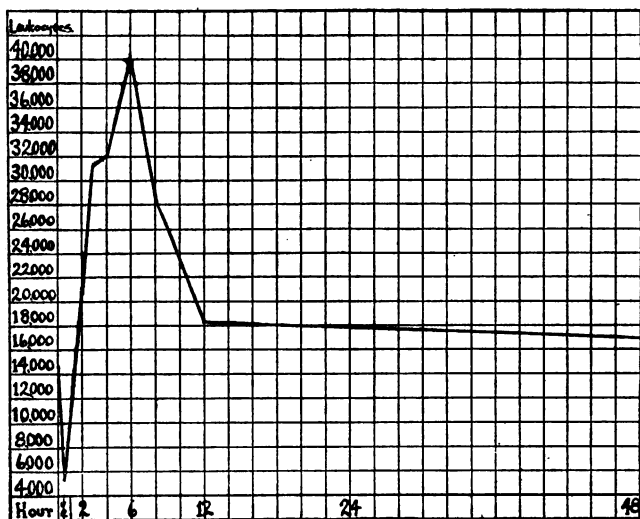


Fig. 2.—Composite leukocyte curve following forty-three injections in twenty-four cases of acute articular rheumatism.

fall in the leukocyte count. The count may fall to normal or below, resulting in a leukopenia, but a leukocytosis soon follows. During the first hour after the injection, and especially at the time of the chill, there is a rise in blood-pressure. After the chill the blood-pressure falls, reaching a maximum drop of 92 systolic and 60 diastolic, about six hours after the injection, and then coming up gradually to nearly normal in forty-eight hours.

A differential count of the leukocytes shows that fol-

lowing the injection there is a steady rise in the neutrophils from the first, reaching a maximum point two or three hours after the injection and then falling gradually for about forty-eight hours to a percentage slightly lower than before the injection. There are minor changes in the lymphocyte and the eosinophile count.

No marked change was seen in the urine following the injection.

Besides patients with chronic and acute arthritis, three with lobar pneumonia received the vaccine. Early cases in the second or third day were chosen, and a similar reaction occurred, except that the temperature instead of remaining low after the injection gradually rose again in forty-eight hours to about the same level as before, where it continued until the natural crisis. No changes were noted in the physical findings following the injection. Intravenous injections of vaccine are contraindicated, Scully says, in those cases in which the vasomotor system is weakened, and when the nervous system is unstable. In these cases collapse may occur with the possibility of death resulting. In acute infections, as lobar pneumonia, small doses are advisable because of the weakened cardiac musculature.

In giving the results the author says that in twenty-five cases of acute articular rheumatism treated with vaccine, ten cleared up after a single injection. All were recent and uncomplicated cases. No recurrences were noticed when under observation nor did any of these patients return to the hospital. Three cases cleared up slowly, requiring two or three injections. Two cases recurred ten days after clearing up nicely after the first injection. These patients remained well after a second injection. Four patients presented complicated conditions, two with endocarditis, one with pericardial effusion, and one with empyema. In these cases there was a continued high temperature, and the patients received only temporary improvement after the vaccine until placed on salicylates. Four other cases were resistant to vaccine, and cleared up under intravenous injections of sodium iodide.

[At present the trend is distinctly away from specific

vaccine therapy, because of such recent work as reported by Jobling, Miller and others in the injection intravenously of protein split-products. Theobald Smith's early insight into the cause for the effectiveness of vaccines is becoming more evident. Whatever specific effect specific vaccines seem to have, they have because they are really foreign proteins.—GEN. ED.]

A Clinical Thermometer Essentially Therapeutic and Adapted to Military Needs. Many devices need improvement or reconstruction to meet war's demand for practical efficiency, among them the clinical thermometer. This indispensable little instrument has been but little improved upon within the last thirty years, though employed constantly by every physician and nurse. Now is the logical time to make those reasonable changes which the conservatism of the medical profession would render difficult of adoption except under extraordinary influences.

E. O'Neill Kane,³ first lieutenant M. O. R. C., proposes that the scale of the instrument under consideration be especially constructed with a view solely to recording the human temperature. To attain this end, the normal human temperature should be indicated, he thinks, by zero instead of 98.6° Fahrenheit, or 37° Centigrade, and the deviations as indicated by the mercury above and below normal should be made to read plus and minus therefrom.

This idea of fixing the normal temperature of man as the zero of the clinical thermometer is not original with Kane. Dr. Seguin, nearly fifty years ago, devised this reading for his surface thermometer, and Hunstock and Chavez patented an instrument with a like scale in 1889. Doctors are loath, however, to step from the beaten path. They have a proper antipathy to patronizing patented ideas and inventions, and are too modest to assert their right to an instrument exclusively their own. This is the reason, Kane thinks, for the irrational adaptation of a thermometer, made for use in the arts, to the requirements of medicine, patiently tolerated by sen-

(3) Paper read at meeting of the West Branch Medical Association, at Hecla Park, near Bellefonte, Pa., Aug. 24, 1917.

sible men despite the inconvenience. Much perplexity would be saved the inexperienced reader by so simple an improvement, and the surgeon, too, would find less difficulty in making the patient or attendant comprehend the meaning of deviations from the normal. Even experienced nurses and physicians would be saved the conscious or unconscious effort in the calculation now necessary to determine quickly the exact hypo- or hyperpyrexia of the invalid. Kane would even recommend the still more radical step of creating a standard of degrees also peculiarly our own. Thus, we might utilize the difference in temperature between the axilla and the mouth or rectum. Besides being a standard formed on an essentially human basis, this would be found convenient for ready reference and adjustment.



Other improvements upon the instrument, though of minor importance, are worthy of suggestion. A luminous background (radiumized) with clearly indicated figures and cross-lines, would be found particularly useful for night-reading (a feature of no small advantage to the military surgeon when, for any reason, as, for instance, the fear of night aerial attacks or the necessity of use in improvised trench hospitals, it is advisable to avoid a light, or when lights must be extinguished to prevent detection by the aviators of an opposing enemy). Markings on such thermometers could be more easily read if the instrument were larger. A larger instrument, too, made of heavy glass, though less sensitive and therefore requiring a longer time for accurate reading, would be less likely to break. And this suggests the advantage of having it reinforced at the place where it comes in contact with the teeth, thus preventing it being broken or bitten off by an ignorant or delirious patient, and at the same time serving as an indication point to the attendant of the distance which the mercury should be thrust under the tongue.

TYPHOID AND PARATYPHOID FEVER.

Method of Isolating the Bacteria. Chiefly because of the dispute that has arisen among bacteriologists in regard to the value of brilliant green and telluric acid in media used for the isolation of typhoid and paratyphoid bacilli, Archibald Leitch³ publishes the result of his experience with this media in one of the war hospitals in Britain.

The method was first used by Browning, Gilmour and Mackie, who, as a result of experiments with various dyes concluded that brilliant green in very weak solutions, had an especially inhibitory effect on the colon bacillus as contrasted with typhoid and paratyphoid bacilli, while it had a powerful bactericidal action on practically all other organisms.

These authors found that in addition to brilliant green the presence of telluric acid in their medium reduced still further the number of organisms other than those of the typhoid group giving the ordinary sugar reactions of the enteric group, but differing from them in fermenting inosite. Leitch has therefore used both brilliant green and telluric acid in media used in the work reported here. Even with both of these he says that organisms may be obtained which survive the inhibitory action and which still do not belong to the typhoid or paratyphoid group, so far as can be determined by the ordinary tests.

The number of such organisms present, however, are greatly reduced as compared with the number encountered in making direct plate of material suspected of containing typhoid bacilli.

The work carried out by Leitch was that of testing feces and urine of convalescent soldiers for typhoid and paratyphoid bacilli with the idea of weeding out any typhoid carriers who might return to camp. From the results which he obtained, he says that he would have no hesitation in preferring the brilliant green method alone if he were confined to a choice between that and the MacConkey plate, but the use of the two, where it is possible, would be nearer an ideal.

(3) Brit. Med. Jour., Sept. 2, 1916.

By the use of brilliant green a great deal of unnecessary work is disposed of by throwing out large numbers of "likely" colonies that would turn out in the long run to be quite useless for the purpose desired; and also there is entire suppression or a great restraint of the growth of organisms normally found in feces and urine. And, above all, one may succeed in obtaining pure growths or numerous easily identified colonies on plates of the organisms for which search is made.

The routine technique adopted by this author for the examination of feces is to emulsify a small mass in peptone broth by shaking up a roughly pea-sized portion with 5 c.c. of bouillon. A drop of this is taken and spread on bile-salt agar plates by means of a glass spreader. The broth emulsion is then allowed to stand for a few hours in the incubator, and at the end of that time two loopfuls of the supernatant fluid are transferred to tubes of brilliant green peptone water with the dye in a concentration of 1 in 200,000 (that is 0.5 c.c. of 1 per cent. aqueous solution, of brilliant green to 1 liter of peptone water). To this is added telluric acid in the proportion of 1 to 25,000, and the addition of this acid does not effect the reaction of the medium.

After incubating this telluric-acid, brilliant-green medium inoculated from the broth cultures for 18 hours, it is then plated on MacConkey's medium and the colonies examined after further incubation.

Leitch advises that the feces be not put directly into the brilliant-green peptone water, as the medium is usually decolorized, and when this occurs the growth of colon bacilli is not inhibited. It is for this reason that the feces are first shaken up with broth, and the broth after the above-named time of incubation transferred to the brilliant-green media.

When likely colonies are obtained the same routine is adopted as in the case of the direct plate. They are transferred to lactose peptone water. If after forty-eight hours no fermentation results, the organism is tested on glucose, mannite, dulcete, maltose and broth and then submitted to the final test of agglutination by specific serums.

The accompanying table presents the results of the

examination of 1,023 specimens. It is said that in this work when the material was plated directly not a single

RESULTS OF THE EXAMINATION OF 1,023 SPECIMENS.

Result.	No. of cases with likely colonies.	Lactose fermenters.	Carried to other sugars.	Necessary agglutination tests.	Actual positives.
By direct plating.	373	59	314	161	17
By brilliant green and telluric acid	120	39	81	45	21

instance was observed in which pure growths was obtained. There were always mixed cultures of different bacteria. By the brilliant-green method, however, there were pure growths of colorless colonies in sixty-two cases.

In no single case by direct plating was the plate sterile, whereas 50 per cent. of plates by the indirect method showed no growth whatever. This means an enormous saving of time. By the direct method, six cases of dysentery organisms were found in addition to the typhoid, whereas only one was discovered by the brilliant-green method, for dysentery bacilli are likely to be killed off by brilliant green.

In the examination of urine for typhoid and paratyphoid bacilli, an interesting experiment was carried out as follows:

The urine of a carrier in which *B. paratyphosus A* and *B. coli* could be demonstrated by the ordinary straight plating method was added to the urine of fifteen other patients in the proportion of 1 to 10. Two series of these dilutions were made, and to one was added brilliant green in concentration of one in 250,000. After twenty-four hours' incubation, plates were spread with the result that by the direct method in only one case was the paratyphoid organism recovered, though *B. coli* were found in abundance on all plates, while by the interposition of brilliant green there was found the paratyphoid organisms in nine cases and these in practically pure cultures.

The method of Browning, Gilmour and Mackie is therefore considered a useful one in detecting a number of carriers of typhoid, or paratyphoid that are liable to be overlooked by the ordinary procedure. Both methods

Leitch says, should be done together as a check on each other. Owing to the saving of time, if one method alone has to be used it should be that which makes use of brilliant green and telluric acid.

Isolation of Bacilli from Ear Discharge. Two instances in which typhoid bacilli were isolated from a purulent discharge from the middle ear are cited by A. D. Bennett⁴ of Washington, D. C.

One patient was a man 34 years old, who had suffered from typhoid while serving in the United States Army in Porto Rico in 1898. From the time of his recovery to the date of this article he had had intermittent attacks of purulent otitis media, and along with several other organisms obtained in this pus were typhoid bacilli. These were isolated on several occasions and treatments with typhoid vaccination were given, following which the case improved decidedly. The final outcome of the condition was not known because the patient was lost track of.

The second case was that of a girl 15 years old, who had suffered in her early years from diphtheria, measles, chicken pox, had had tonsils and adenoids removed, had had scarlatina, and what had been termed typhoid-pneumonia. The acute otitis media for which she consulted Bennett was of one month's duration, and in the pus discharging from the left ear were found, among other organisms, typhoid bacilli.

The author was unable to learn of any case of typhoid fever that had resulted from contact with these patients. Because of the unusual character of such typhoid carriers he makes this report.

Differentiation of Agglutinins in Typhoid. An attempt has been made to distinguish between agglutinin produced by prophylactic inoculations with typhoid, paratyphoid and cholera organisms, and agglutinin produced by infection with live organisms, by a comparison of the differential count of the leukocytes with the agglutination titre. This work was carried out by I. Walker Hall and D. C. Adams.⁵ They tabulate the result of a large number of agglutinin determinations and differ-

(4) Jour. Amer. Med. Ass'n., Dec. 30, 1916.

(5) Lancet, Sept. 16, 1916.

ential counts of leukocytes on patients suffering with typhoid and paratyphoid, and also on people who had received prophylactic inoculation.

In a summary of their results, it is stated that they have not observed the distinct eosinophilia which they expected to find; in fact the eosinophile percentages did not exceed those that had been encountered in routine examinations of other forms of convalescence. This feature does not seem to offer much aid in the differentiation of an inoculation and an infective agglutinin when only agglutinin is present in the blood.

With regard to other types of cell, the evidence accumulated at all events, suggests that extended observations with the addition of other important hematologic procedures may show that some information will be gained by the examination of blood films in cases of difficulty, and especially when we have to deal with continuous fever in men who have been inoculated with mixed vaccines against typhoid, paratyphoid *A* and *B*, and cholera. So far as the authors were able to determine, it seems probable that when the agglutinin present was due to inoculations, the blood films yielded approximately normal figures, while in case of an infective agglutinin the typical leukocytosis or polynuclear leucopenia associated with the causal organism was found.

They believe that the counts obtained from recently inoculated healthy men, should they be confirmed, would lead to the supposition that the cells which react to dead typhoid and paratyphoid bacilli may prove to be of a different order from those which act upon living infective typhoidal organisms.

Agglutinating Power of Sera against *B. Typhosus* and *B. Enteriditis*. An investigation of the agglutinating properties of sera sent to the laboratory for Wassermann tests was made by Thomas T. O'Farrell,⁶ of the University College, Dublin. The organisms upon which the agglutinating power of the sera were tried were *B. typhosus*, *B. paratyphosus A* and *B*, and *B. enteriditis* Gaertner (Delépine, 7160). The sera were dealt with in routine manner as they were received. With regard to antityphoid inoculation they were classified as follows:

(6) *Lancet*, Dec. 9, 1916.

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Group II.—Sera of men about whom information as to date of last inoculation only was obtainable	127
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Four hundred and ninety-five sera were examined, and in 270 instances in which the subject had been inoculated 87.1 per cent. gave positive agglutination for *B. typhosus*. Of these, the greater number gave up to 25 standard agglutinin units per 1 c.c. of serum; after this the percentage of units obtained dropped rapidly until the number of sera containing more than 125 agglutinin units formed but quite a small percentage of cases.

During the first month after inoculation the maximum number of agglutinin units was obtainable. This maximum falls rapidly during the third month after inoculation. Between the fifth and fourteenth months a fairly high agglutinin unit content may be met with, but after fifteen months subsequent to inoculation the agglutinin units were not found above 100.

There was some evidence to show that after the highest point in the agglutination, following antityphoid inoculation, had been reached the subsequent fall was progressive, but was inclined to remain steady or even to rise slightly at intervals so as to form secondary waves on the downward course. This was more marked in the earlier months following inoculation than in the later months.

The sera of men inoculated twice gave more positive reactions than men inoculated only once. Also a greater number of them gave 25, 50 and 100 agglutinin units. Higher titres were obtained with the sera of men inoculated twice during the second, third and fifth months after inoculation than among those who had been inoculated once.

The presence of syphilis (as indicated by a positive Wassermann) does not affect the agglutinating power of

a serum for *B. typhosus*, though apparently it does increase slightly its power to agglutinate *B. enteritidis*, 7160.

The agglutinating power of a serum for 7160 is not influenced by antityphoid inoculation.

Out of 366 sera, consisting of both inoculated and non-inoculated men who had either had or were suspected of having syphilis, 19.6 per cent. agglutinated *B. enteritidis* Gaertner (Delépine, 7160) when a 1 in 25 dilution was used. A much smaller percentage may agglutinate this bacillus up to a 1 in 250 dilution. None of these sera was found to affect 7160 in a higher dilution.

Of thirteen men with a previous history of typhoid fever only 3 agglutinated 7160. These men had had typhoid fever 8, 10 and 18 years, respectively, previous to the date of examination. The ten cases not agglutinating 7160 had histories of typhoid fever from four months to twenty-two years previously.

Any of the sera clumping 7160 which were examined for co-agglutinins for *paratyphosus A* or *B* proved negative.

Cultural Differentiation of Typhoid and Paratyphoid A and B. This article gives the method that has been adopted in the laboratories in Cambridge, England, for cultural differentiation of these organisms. The method was worked out by Sydney W. Cole and H. Onslow,⁷ the attempt being prompted by the need of some such convenient scheme in the base hospitals in France.

This work dealt chiefly with the reactions produced by the organisms named on different culture media. The following facts were established:

An acid reaction is produced rather sooner by paratyphoid B. (and B. coli) than by typhoid and paratyphoid A. With phenol-sulphone-phthalein as the indicator the change is seen earlier and is much more sharply defined than when litmus is used.

When excessive production of acid is prevented by using low concentrations of glucose, the reversal to an alkaline reaction is most rapid with paratyphoid B and slowest with A. The fact that A does finally render

(7) Lancet, Dec. 16, 1916.

this medium alkaline is worthy of note, since on litmus milk *A* gives a slight permanent acidity.

When incubated for twenty-four hours in "tryptic broth" containing 0.2 per cent. glucose, *B* produces an alkaline reaction to phenol-sulphone-phthalein, while typhoid and paratyphoid *A* give acid reactions. This difference is so marked and so constant that it has been adopted as the basis of the method for the cultural diagnosis of paratyphoid *B* from typhoid and paratyphoid *A*. It is conditional on the size of tube and volume of fluid specified in the description of the method given below.

When incubated in "tryptic broth" containing 0.1 per cent. glucose for twenty-four hours, paratyphoid *B* and typhoid cause an alkaline reaction to phenol-sulphone-phthalein, while paratyphoid *A* gives an acid reaction.

The following rapid cultural method for differentiating these organisms was finally adopted:

Two solutions are employed, a glucose solution ("G") and a dulcitate solution ("D"). The former is used for differentiating *B*. from *T*. and *A*., since at the end of twenty-four hours *B*. is alkaline while the others are acid. The solution "D." differentiates *A*. from *T*., since at the end of twenty-four hours *A*. is acid and *T*. alkaline. The solutions required are as follows:

GLUCOSE SOLUTION "G."

"Tryptic broth"	1000 c.c.
Phenol-sulphone-phthalein (0.04 per cent.)	40 "
Glucose	2 gm.

Tube in 3 c.c. portions, and sterilize by steaming for twenty minutes on three successive days. Tubes of $\frac{3}{8}$ in. diameter are used. This size must be adhered to in order to obtain the desired differentiation, for with a decrease of diameter the rate of alkali production is retarded, with an increase it is accelerated. This is due to the effect of the diameter of the tube on the surface area, and therefore on the supply of oxygen.

DULCITE SOLUTION "D."

T/6	1000 c.c.
Phenol-sulphone-phthalein (0.04 per cent.)	40 c.c.
Dulcitate	2 gm.

Tube in 2 c.c. portions in tubes of $\frac{5}{8}$ in. diameter, and sterilize by steaming as before. A glass bead is usually added before sterilizing to distinguish these tubes from "G." Tubes containing 0.5 per cent. sucrose and 0.5 per cent. lactose, and fermentation tubes containing 1 per cent. glucose are also kept ready for use. These sugars are dissolved in T/6, and pheno-sulphone-phthalein is added in the proportion mentioned above. Any other carbohydrate solutions required in the particular routine employed are advantageously made up in the same way.

After plates have been grown from feces or other material in the usual manner, suspicious colonies are emulsified into a tube of glucose broth. This tube is then incubated for two hours. Two loops of this are then sown into a tube of "G." and "D." as well as the other sugars employed. These tubes are then incubated for exactly twenty-four hours at 37° C. The tubes are now inspected, and can be examined for motility if this has not already been done. Should the presence of typhoid, or paratyphoid *A*, or *B*, be indicated by the reactions of the lactose-sucrose and glucose fermentation tubes, the final differentiation can be decided by the reactions in "G." and "D." After twenty-four hours they are as follows:

Organism.	Solution "G."	Solution "D."	Glucose fer- mentation tube.
<i>B. typhosus</i>	Yellow	Red or pink	Acid
<i>B. paratyphosus A</i>	Yellow	Yellow	Acid and gas
<i>B. paratyphosus B</i>	Red or pink	(Variable)	Acid and gas

The change of reaction undergone by *B* in solution "D." seems to be variable, but this is of no importance, since its presence can be ascertained from solution "G." In some cases acidity is reached in the space of three or at the most four hours, whereas in others so great is the capacity for alkali production during the initial stages that the dulcete never affords sufficient acid to change the reaction. On the other hand, the behavior of *A* after the first twenty-four hours is quite distinctive, and confirmatory evidence of its presence is obtained by allowing the tubes to remain an additional forty-eight hours in

the incubator. Under these circumstances it is found that *A* remains a bright yellow until the middle of the third day. By this time typhoid and paratyphoid *B*, as well as the large majority of the non-pathogenic fecal organisms, show distinct alkalinity.

The authors have not succeeded in finding a cultural distinction between *B. paratyphosus B* and *B. enteritidis* Gaertner. In this method, as in all others, the final test is agglutination against specific sera.

The Value of the Agglutinating Power of Serum from Individuals Inoculated Against Typhoid and Paratyphoid. In this report to the medical research committee, G. Dreyer and E. W. A. Walker,⁸ state that the agglutinin reaction constitutes the most valuable guide which we possess at present for the diagnosis of the enteric fevers (typhoid, paratyphoid *A*, and paratyphoid *B*). While the direct cultivation from blood, feces, and urine is, when successful, final and convincing, the percentage of cases in which positive results are obtained by culture methods does not at a liberal estimate exceed about 60 per cent. Among these cases will, of course, also be included carriers not actually suffering from the active disease.

Unfortunately, there appears to exist a belief that the introduction of protective inoculation against *B. typhosus*, and more recently against the paratyphoid bacilli, also, has rendered the agglutinin reaction less reliable or less conclusive diagnostically than was formerly the case. This belief, however, is not justified by the evidence available; though it is undoubtedly the fact that the practice of inoculation has not only enhanced certain difficulties which already existed, but also introduced some new difficulties of its own. As a result of this it is no longer possible to make use with advantage of certain methods largely qualitative in character which before were commonly considered adequate for diagnostic purposes. And it has become necessary to employ some accurately quantitative method. Moreover, since the diagnosis now depends on the results of a series of several (three or more) successive observations, the method used must be one whose results on successive occasions

(8) *Lancet*, Sept. 2, 1916.

are strictly comparable, and can be expressed in definite and accurate measurements relative to some fixed standard. Such a method has the further great advantage that wherever and whenever such tests may be performed they will form a part of homogeneous statistical material. It is said that all these requirements are met by the method which has been rendered generally available in naval and military hospitals for the past twelve months, by the issue, on behalf of the Medical Research Committee, of the standardized agglutinable cultures prepared in Oxford.

It is stated further that the curious and widespread lack of appreciation which still exists with regard to the necessity for employing exact quantitative methods in performing agglutination tests in inoculated individuals led to most remarkable and contradictory statements. Reference is made here to reports of C. D. Hamilton and H. L. Tidy which has been discussed in other current reviews. The opinions expressed by these two authors are, respectively, that "a positive Widal reaction in any person who has ever been inoculated with the antityphoid vaccine is of no value in diagnosing typhoid fever" and that a positive agglutinative reaction to *Bacillus typhosus* after the fifth day of pyrexia is as definite a proof of typhoid fever in an inoculated man as in a non-inoculated one. The burden of the present article is to show that a positive Widal reaction from the serum of a previously inoculated individual does not rule out the possibility of making an accurate diagnosis of typhoid fever or paratyphoid fever, and to show that the presence of pyrexia does not destroy agglutinin produced by previous inoculation. Much emphasis is placed upon the plotting of the agglutinin titre in a serum as a curve and comparing the time of maximum agglutination with the clinical course of the disease. In a certain number even of the mildest cases of these infections the rise and subsequent fall in the agglutination titre are so definite that the diagnostician could never be in doubt; but in other cases the rise and fall of the curve are much less marked, and differences of opinion exist as to whether the case is one of active infection or not. In order to assist in the elucidation of such cases it may be stated

that the following points are of importance in the interpretation of the agglutinin curves.

The maximum agglutinin titre of active typhoid or paratyphoid infection occurs between the sixteenth and twenty-fourth day of the disease, and most frequently about the eighteenth to twentieth day.

If the maximum is reached at what appears to be an earlier date, it is important to institute a careful inquiry into the actual date of onset of the illness.

If it is clear that the maximum falls markedly outside the limits given above (day 16-24) a diagnosis of typhoid or paratyphoid fever should not be based on a rise in titre of only moderate extent—i. e., a 100 or 200 per cent. increase in agglutinin titre. Because experience is not at present sufficient to exclude the possibility that a rise of this extent may be due to other febrile conditions.

In following out the titration of the patient's serum on several successive occasions it will frequently be found that the maximum has fallen between two dates of observations. And two successive observations at about the same level do not mean that the curve is stationary at this point, but merely that the maximum has occurred between there. Similarly, if the two highest observations are at different levels, it does not follow that the highest titre observed represents the maximum of the agglutinin curve. But it does follow that the maximum has occurred between these points.

In inoculated persons among whom mild and atypical attacks of typhoid (or paratyphoid) fever are likely to occur with fever of perhaps only a few days' duration, and with few if any of the usual symptoms, the diagnosis of typhoid or paratyphoid fever must not be rejected without the most careful consideration. So far as experience at present goes, if a regular rise and subsequent fall, even of only 100 or 200 per cent., occurs in the typhoid (or paratyphoid) agglutinin titre of the serum, and its maximum clearly falls between the sixteenth and twenty-fourth day from the onset of illness, the case is likely to be one of typhoid (or paratyphoid) infection. And we must not be misled by the fact that the patient may be convalescent or quite well again long

before the date when his maximum agglutinin titre is reached.

Agglutination Curve in Diagnosis. The agglutination curve and its importance in the diagnosis of typhoid and paratyphoid fevers in inoculated persons is discussed by Georges Dreyer and A. C. Inman.⁹ The work upon which this article is based was performed in the spring of 1915. Along with the report of these results the authors give an account of some of the materials and methods used that should be of decided value to those interested in this phase of typhoid work.

Standard Agglutinable Cultures are prepared of definite opacity and measured agglutinability from strains of the bacilli concerned which have been specially selected for their high specificity. In successive batches of standard agglutinable culture the relative sensitiveness to agglutination of the bacilli contained is indicated by a figure—the so-called *Reduction Factor*—the original standard agglutinable cultures having been arbitrarily given the figure 2.5 as reduction factor. The reason for this will appear immediately in connection with the *standard agglutinin unit*.

Standard Agglutination is the degree of agglutination present in the highest serum dilution in which marked agglutination without sedimentation can be seen by the naked eye.

The Standard Agglutinin Unit is that amount of agglutinating serum which when made up to 1 c.c. volume with normal saline solution causes standard agglutination on being mixed with 1.5 c.c. of the original standard agglutinable culture and maintained at 55° C. for two hours (in the case of dysentery agglutination four and one-half hours) in a water-bath, followed by from fifteen to twenty minutes at the room temperature.

The Reduction Factor.—The total volume in which the reaction occurs being 2.5 c.c. (1 c.c. of serum added to 1.5 c.c. of standard culture) the original standard agglutinable culture was given the reduction factor of 2.5 to express the sensitiveness to agglutination of that particular culture. All subsequent batches of culture have been given reduction factors calculated on this

(9) *Lancet*, March 10, 1917.

basis, thus securing constancy in the agglutinin unit. For example, if a batch of standard culture proves to be twice as sensitive to agglutination as the original standard, so that half the amount of serum produces standard agglutination under test conditions the new standard culture is given a reduction factor of double the size of the original factor—i. e., 5. Thus, whatever be the particular standard culture used to test any given serum the number of agglutinin units found per cubic centimeter of the serum remains always the same, although the dilutions in which standard agglutination occurs will be different. Since when standard agglutination occurs in a serum dilution of 1 in x , then x divided by the reduction factor for the particular standard agglutinable culture used gives the number of standard agglutinin units contained in 1 c.c. of the serum concerned.

“Readings.”—Owing to the rate at which the dilution increases in the series of tubes employed it will commonly happen that no tube in the series exhibits standard agglutination. If this be so, it will be found in looking along the series that while one tube shows strong agglutination with sedimentation the next succeeding tube shows no agglutination or only a trace. In such cases standard agglutination lies approximately midway between the two dilutions. The principal terms employed in describing the different degrees of agglutination met with are “total” (t), “standard” (s), “trace” (tr), and “nil” (0). *Total* agglutination indicates the condition in which the whole, or practically the whole, of the agglutinated bacteria have settled down at the foot of the tube. *Standard* agglutination has already been described; the term *trace* is applied to a very fine granulation recognizable by the naked eye. Around these main terms subsidiary differences congregate themselves as follows: *Total minus* (t—) marked deposit, but a number of floating flocculi remaining in the fluid. On each side of “standard” we find *Standard plus* (S+) and *Standard minus* (S—) respectively. In the former no deposit, but much larger flocculi than are seen in standard agglutination. In the latter finer agglutination than standard, with more the appearance of granula-

tion in the fluid. Similarly, we recognize a *Trace plus* (tr +) and a *Trace minus* (tr —), the former representing something more than *trace* but less than *standard minus*, the latter being on the limit of naked-eye

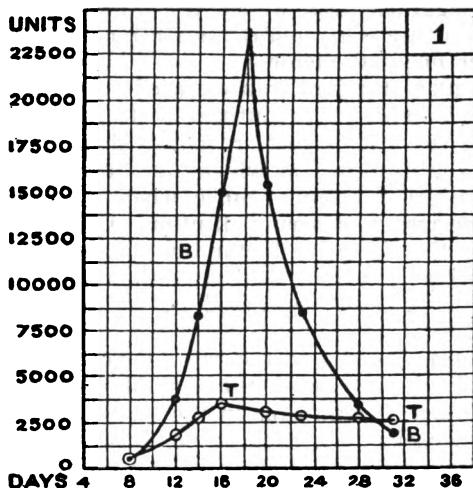


Fig. 3.—*Paratyphoid B* occurring in a typhoid-inoculated individual. The *B* agglutinins rise rapidly from the first observation on the eighth day of the disease and reach the very high level (unusually high) of more than 15,000 units on the sixteenth day. As seen from the shape of the curve the maximum is even much higher than this and is reached about the eighteenth day. Thereafter the usual regular fall sets in at first rapidly, so that the units have fallen from somewhere about 24,000 to 8,600 in the next five days, subsequently more slowly. Meanwhile the typhoid agglutinins have risen very markedly, though relatively much less. They attain their maximum of about 3,500 units about the sixteenth day, some two days before the maximum of *B* agglutinins, falling from this point in a very gradual but quite regular curve to about 2,800 units on the twenty-third day. After the thirtieth day *B* agglutinins, though still much higher than their level at the first observation, have fallen below the typhoid agglutinins, the titre in the two cases being 1,800 units and 2,500 units respectively, showing the greater persistence of the rise produced in the typhoid-inoculation agglutinins as the result of paratyphoid *B* infection than in the *B* agglutinins themselves.

visibility. Finally, on occasion it can be difficult to decide with certainty whether a given tube is absolutely *nil* or not, the term *query trace* (tr ?) is then applied."

With this information it is seen at once how the accompanying curves (Figs. 3, 4, 5) were obtained and

also how the maximums as found and plotted here are of distinct value in making a diagnosis by means of agglutination tests on patients who have been inoculated for typhoid and paratyphoid. It is also shown how

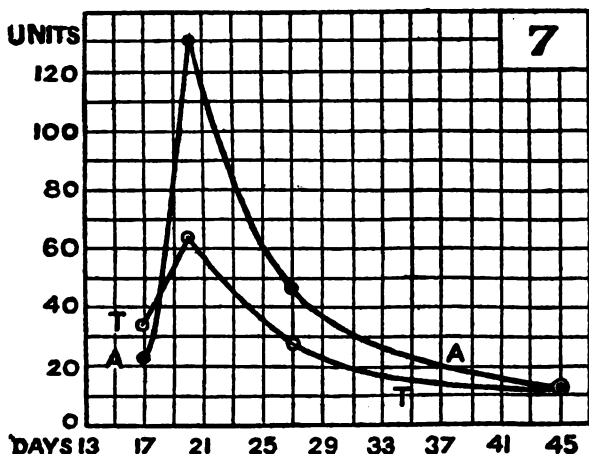


Fig. 4.—*Paratyphoid A* in a typhoid-inoculated individual. The agglutinins rise rapidly from about 20 units on the seventeenth day of the disease to their maximum of about 130 units on the twentieth day. Thereafter they fall rapidly to reach the level of about 45 units on the twenty-seventh day. The further course of the curve is shown in the chart. The typhoid agglutinins show a marked relative rise and fall with a maximum of about 64 units on the twentieth day. The fall is less steep than that of the *A* agglutinins.

entirely misleading it would be to draw conclusions from a single observation of the height of the titre, since in many instances the titre for the infecting organism may be found less than that for the inoculation agglutinins, and may indeed be lower throughout the whole infection. On the other hand, it is certainly the case that at its maximum the titre for the infecting microorganism will *usually* exceed the titre of inoculation agglutinins even though these may be greatly raised as a result of the infection. Nevertheless, as the fall in titre proceeds the curve of paratyphoid *A* and *B* agglutinins falls more rapidly than the curve of typhoid inoculation agglutinins, so that the latter is cut by the former at some points in the fall.

The maximum agglutination titre for the infecting organism most frequently occurs about the eighteenth to twentieth day, and almost always lies within the limits sixteenth to twenty-fourth day of the disease.

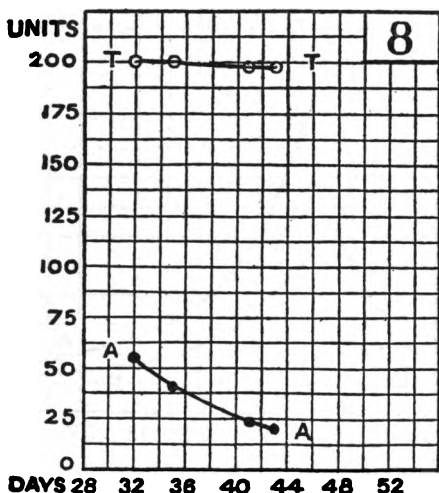


Fig. 5.—*Paratyphoid A* in a typhoid-inoculated individual. *A* late case. The typhoid agglutinins are at a high level, remaining practically unaffected by the *A* infection at a titre of about 200 units. The *A* agglutinins show a steady fall from 56 units on the thirty-second day of the disease to 20 units on the forty-third day.

As regards the effect of active paratyphoid infection on the typhoid inoculation on agglutinins one of three things may occur: (a) The titre may remain unchanged throughout the infection; (b) it may undergo a rise of moderate extent; (c) it may undergo a marked rise. When such rises occur it is found that they are either synchronous with or antecedent to the rise of agglutinin titre for the infecting microorganism, and that the maximum falls somewhat earlier than the maximum for the infection agglutinins (or occasionally at about the same time). The change in typhoid inoculation agglutinins associated with paratyphoid infection is in general much more marked in the case of paratyphoid *B* than in the case of paratyphoid *A*.

In view of what has here been shown, it is obvious that it would be quite futile to try to fix a limit of agglutination titre for T.-inoculated individuals, and to proceed to diagnose cases which showed higher titres (even many times higher) as cases of active typhoid infection. The final guide in all these cases of enteric infection is the relative extent of the rise and fall in agglutination titre for the organisms concerned, together with period when the maximum titre is reached.

The conclusions reached by H. L. Tidy, captain in the British Medical Corps, are spoken of by Georges Dreyer, Alex G. Gibson and E. W. Ainley Walker¹⁰ as unfortunate. They are so termed because, if accepted, they would have a most disastrous effect on diagnosis, and on the estimate of the protective value of inoculation. These authors quote Tidy's conclusion as follows:

The inoculation agglutinins are diminished or entirely removed by febrile conditions. It is possible that they are converted into agglutinoids.

In certain cases they may return, but usually do not return.

A positive agglutination reaction to *Bacillus typhosus* after the fifth day of pyrexia has the same value in an inoculated as in an uninoculated person.

Immunity conferred by inoculation may be affected at the same time as the inoculation agglutinins.

It is the opinion of Gibson and Walker that these conclusions can readily be shown as fallacious. It is said that they are based upon a small number of cases, and the authors present tabulated results obtained by doing agglutination tests on many cases of typhoid and paratyphoid fever which enable them to make the following statements:

First, the febrile condition associated with paratyphoid fever does not cause disappearance of typhoid agglutinins from the blood of persons inoculated against typhoid.

Second, other febrile conditions, also, in so far as they have hitherto presented themselves do not cause disappearance of typhoid agglutinins from the blood of inoculated persons. Third, a statement that the posi-

(10) Lancet, April 8, 1916.

tive agglutination reaction to *Bacillus typhosus* after the fifth day of pyrexia has the same value in an inoculated as in an uninoculated person is entirely erroneous. Its acceptance would lead to such deplorable results in diagnosis that the authors feel it unnecessary to repeat the denial.

They say that if Tidy's novel views were to be seriously applied in serodiagnosis the majority of persons inoculated within a year or so, who suffered from five days' pyrexia, would necessarily be returned as cases of typhoid infection when examined by a reliable agglutination technique.

The Typhoidin Reaction. A test of the accuracy and reliability of the typhoidin reaction has been made by E. S. Kilgore,¹ of San Francisco. He says that it has been found that with the dry preparation of typhoidin there were average differences between groups of immunes and non-immunes, but that the differences were small in comparison with the variation among individuals in the same groups, so that the test had little value for the individual case. The desirability, therefore, became apparent of examining possible sources of variability in the results of the tests other than differences in typhoid immunity.

The technique was the ordinary von Pirquet technique. As is ordinarily done, the results in this work were recorded as a quotient, and this represented the factor obtained by dividing the diameter of a test areola by that of the control. In a comment on the work the author states that the facts brought out by it indicate even more strongly than has been reported formerly, that the cutaneous typhoid tests should not be relied on as an index of immunity in individual cases, and that even in a study of groups of cases the results need to be considered with much conservatism. It was found that each of the following factors contributed to the inaccuracies in the readings in about the proportion given:

Indefiniteness in areola outlines, 5 per cent.

Effect of scattering the readings over several hours,
3 per cent.

Effect of participation by many observers, 4 per cent.

(1) Archiv. Int. Med., February, 1917.

Effect of variation in the trauma, etc., 6 per cent.

The author concludes that this series of cases has emphasized the total unreliability of the cutaneous typhoidin test in its present state of development as an index of typhoid immunity in persons and the need for much caution in interpreting its results even in a considerable series of cases.

The reasons for this unreliability appear to be, first, unavoidable variations in the application of the test; second, indefiniteness of the readings; and third and most important, the relatively large amount of non-specific reaction which is produced by typhoidin—upward of three times the amount that can be attributed to specific disturbances among the subjects.

In varying degrees, similar sources of inaccuracy undoubtedly exist for other cutaneous tests and should be investigated.

According to the opinion of this author: the dry typhoidin is little affected by age; the typhoidin test when applied intracutaneously in a dilution of 1 to 100 and read twenty-four hours later is without value.

Further studies of this reaction have been made by John N. Force and Ida M. Stevens², who summarize their results as follows:

A stable preparation of typhoidin may be rapidly prepared by precipitating a concentrated broth culture of *B. typhosus* with 95 per cent. alcohol, and subsequent dehydration with absolute alcohol and absolute ether.

Definite reactions persisting forty-eight hours were produced in human beings by the intradermal injection of 0.05 c.c. of a 1 in 10,000 suspension of typhoidin in phenolated saline. In order to produce a similar reaction in rabbits, a dose of 0.1 c.c. of a 1 in 1,000 suspension of typhoidin was necessary.

It is imperative that no account be taken of the appearance of the reaction at the end of twenty-four hours. A positive typhoidin reaction is indicated by the presence, forty-eight hours after the test, of a well-defined erythematous papule at least 5 mm. in diameter. Out of 108 positive reactions, the forty-eight hour papule

(2) Archiv. Int. Med., March, 1917.

measured 10 mm. or over in twenty-six instances; the average measurement of 108 papules was 8.4 mm.

Out of eighteen normal persons, seventeen gave negative reactions; out of twenty-six persons with a history of typhoid, nineteen gave positive reactions, one gave a doubtful, and six persons (four with questionable typhoid histories) gave negative reactions. Out of 152 persons previously vaccinated against typhoid, twelve of fifty-six vaccinated during 1916, three of eleven vaccinated during 1915, thirteen of twenty-nine vaccinated during 1914, and twenty-six of fifty-two vaccinated during 1913 gave negative reactions.

Ten of thirteen persons showing a negative reaction to the skin test before vaccination (or revaccination) gave positive reactions after vaccination (or revaccination).

The revaccination of previously vaccinated persons showing negative skin reactions produced local or general reactions no greater in intensity than the vaccination of normal persons, and much less severe than the reactions produced by the revaccination of persons showing positive skin reactions.

The routine administration of three doses of typhoid vaccine is in many cases not sufficient to produce sensitization to typhoid protein, and presumptively, therefore, protection against typhoid fever.

Even granting that typhoid immunity is of longer duration than cutaneous sensitiveness to typhoid protein, the disappearance of this sensitiveness furnishes an indication for revaccination of the person and still allows a margin of safety within the as yet indefinite limits of typhoid immunity. There is as yet no evidence that a positive typhoidin test is not indicative of protection against typhoid fever. In two instances at least, in the authors' experience, a negative typhoidin test after vaccination was followed by typhoid infection. They feel justified, then, in proceeding on the original assumption of Gay and Force that this test may be used as a measure of protection against typhoid.

It is stated by J. A. Kolmer and J. H. Berge, Jr.,³ of Philadelphia, that while the bactericidal power of human serums over *B. typhosus* is increased in a cer-

(3) Jour. Immunol., August, 1916.

tain proportion of individuals following typhoid or active immunization with a vaccine, there is no direct relation between the typhoidin skin reaction and the results of bactericidal tests *in vitro*. Agglutinins or complement-fixing antibodies or both are present in the blood serum of the majority of persons reacting positively in the skin test and particularly among those actively immunized, but there is no definite relation between these as either may be in evidence in the absence of the other.

Powdered typhoidin and its control produce severe reactions when injected intracutaneously in doses of from 0.0005 to 0.001 mg.; these reactions, and particularly that produced by the control, render the reading and interpretation of the test quite difficult and subject to much error. Cutaneous anaphylaxis to typhoidin was found by the authors apparently to persist for a longer time among those who have had typhoid than among those actively immunized with the vaccine. Among the latter the highest percentage of reactions was found during the first year following immunization. While the typhoidin reaction indicates sensitization to typhoid protein, Kolmer and Berge think that there is not yet sufficient evidence to warrant its acceptance as an index of immunity in typhoid.

[The last statement represents the best opinion at the present time.—GEN. ED.]

Vaccination Against Typhoid. A comparison of two methods of vaccinating against typhoid fever has been made by Eugene S. Kilgore.⁴ He says that of 15 or 20 recognized methods of immunizing against typhoid fever, the one most commonly used in this country has been that employed in the United States Army, which consists of three injections at seven or ten day intervals, the first of 500 millions and the second and third of 1 billion each of a heat-killed culture of a mild strain of typhoid bacillus. Another method which has been extensively used in California during the last three years, is that introduced by Gay and Claypole. This vaccine consists of an alcohol-killed culture of the typhoid organism which has previously been treated by an immune serum,

(4) Archiv. Int. Med., February, 1917.

the so-called sensitized vaccine. The cultures are then dried and ground, suspended in salt solution and the sediment redried, and weighed amounts are used in immunizing. Experimentally in rabbits such a vaccine was thought to produce more permanent immunity than non-sensitized vaccine, and it was expected to give fewer unpleasant symptoms following human inoculation.

In the summer of 1912, sixty members of the University of California Hospital staff were vaccinated according to the United States Army plan with vaccine obtained through the Letterman General Hospital. The next year about seventy new subjects were vaccinated with sensitized vaccine according to the three-day interval plan, the vaccine being prepared under the direction of Professor Gay of the University of California, in the department of pathology and bacteriology.

Kilgore says that the final conclusions are not warranted from the number of observations in this series, but the following findings may be set forth with the understanding that they are to be given weight only in accordance with the number of observations on which they are based: It was found the higher the typhoidin quotient in a given person, the greater his chances of a severe reaction to antityphoid inoculation. The more severe local reaction to vaccine tends to occur in those subjects with a higher temperature reaction.

The supposedly more severe average reaction to antityphoid inoculation of subjects who have previously had the treatment is probably over-rated. The use of army vaccine or sensitized vaccine sediment, if the preparations are fresh, makes little if any difference in the average local and temperature reactions.

When either type of vaccine is administered every other day, the temperature reactions following the second and third doses are likely to be more severe than when the injections are ten days apart. The difference in the local reactions is not so clear cut. The average impression of the subjects vaccinated every other day is that the second injection gave the greatest local and general discomfort and the third the least. The average member of the ten-day group feels that both general and local reaction were less with each succeeding dose.

The typhoidin test, as applied in this work, failed to show any noteworthy differences in effectiveness in the two-day or ten-day schedules, and, in the first few weeks, between the two vaccines used. Later the typhoidin quotients were higher in those who had received sensitized vaccine, but the differences are not decided enough to support definite conclusions that this is the rule.

According to the typhoidin test, it is suggested that the individuals who react least to vaccination tend to profit most by its administration.

Antibodies in Persons Vaccinated Against Typhoid.

In a study of the antibodies in the serum of persons vaccinated against typhoid fever, K. F. Meyer and E. S. Kilgore,⁵ of San Francisco, state that the growing importance of typhoid immunization, the continued uncertainty in regard to the best type of vaccines, optimum interval between doses, and the interval after which revaccination becomes advisable, as well as the desire of the physicians and laity for a practical test of typhoid immunity, make important any work which may throw light on the subject. Their work is based upon the study of ninety-eight students, nurses, and others connected with the University of California Departments of Medicine, most of them young adults, and all in apparently good health; seventeen had had typhoid fever from three and one-half to twenty-five years ago; twenty-six had received army vaccine from three to eight months previously and thirty-seven had been given sensitized vaccine within the same time.

Agglutination and complement-fixation tests were applied to the serum used in this work. In commenting on the work the authors say that there is nothing in the results which is not in harmony with the long-accepted idea that the estimation of antibodies furnishes no accurate index of the power which the body possesses of defending itself against invasion by typhoid organisms. They note that Garbet and Meyer found that serums of rabbits immunized with sensitized cultures were highly protective, more so than animals treated with non-sensitized preparations, yet this potent serum contained small

(5) *Archiv. Int. Med.*, February, 1917.

amounts of agglutinins and complement-fixing antibodies.

Bacteriolytic experiments were not carried out in the work of the present authors on account of the small amount of serum obtained. It has been determined by other workers that these antibodies behave in many respects similar to the complement-fixing antibodies that have been determined in the present work. They think it clear that too little is known of the serologic or cutaneous tests as indices of typhoid immunity at the present time to make them worth anything when applied to individual cases with the idea of deciding about the need for prophylactic inoculation. Neither can they in their present development form the basis of reliable statistical researches to determine the relative merits of different types of vaccines. From the reviews of the literature, it is also evident, the authors think, that for further advances in the subject we must look to carefully controlled experiments with large numbers of observations. The present series, while it is larger than the majority of those reported in the recent literature, and furnishes fairly definite information and suggestions on certain points, is too small to throw any light on some of the important questions involved.

The authors conclude:

In comparison with army vaccine, sensitized vaccine sediment produces small amounts of agglutinins.

Complement-fixing antibodies are found in about equal amounts in the serum of those who have had army vaccine and those who have received sensitized vaccine.

It has been shown anew that for individual cases serologic and allergic immunity tests in their present form are inconclusive as measures of typhoid immunity.

Preparation of Sensitized Vaccine. In an article on sensitized typhoid bacteria, A. L. Garbat⁶ of New York describes, at considerable length, the process of preparing sensitized vaccine. In speaking of the use of vaccine, he refers first to the ordinary vaccine or suspension of the dead typhoid bacilli. He says that the injection of the dead bacteria into a normal individual is usually followed by the production in great numbers of the

(6) Med. Record, Dec. 30, 1916.

various antibodies, as bacteriolysins, agglutinins, bacteriotropins and, occasionally, complement-fixation bodies. Some of these immune agents, he says, are probably capable of destroying the typhoid bacilli. If the inoculated individual is exposed to infection, that is, if live bacteria find their way into his body, they are readily destroyed, and will not multiply. Naturally, if the army of invaders is excessive or the defense too slight, infection will arise in spite of the prophylactic measure. Fortunately such instances are exceptional. The immunity is, therefore, explained on a bacteriolytic and, to a less degree, on a bacteriotropic or opsonic basis. From clinical experience it has been shown that immunity persists even after these immune bodies can no longer be demonstrated.

The prophylaxis attained by the injection of sensitized typhoid vaccine, according to the Bezredka method, whether the bacilli be living or dead can not, if sensitization is complete, be explained on identically the same principles, for as soon as the sensitized bacteria enter the normal system they combine with the complement of the blood and are broken up. The agglutinating and bacteriolytic antibodies and the complement-fixation bodies are, therefore, either not produced at all or only in very small quantities; consequently, the reliance for protection must be placed on a phagocytic activity, stimulated by the liberated central substance of the broken-up bacteria, the so-called endotoxin. Thus the prophylactic immunity with sensitized vaccine is of a bacteriotropic character, while that with the non-sensitized vaccine is mainly of a bacteriolytic nature. Which one is superior can not as yet be definitely stated. So far, many thousands of patients have been inoculated by the sensitized method, but sufficient data are lacking for comparison with the method of using merely dead bacilli, or the Wright method.

The author thinks that statistics from the treatment of soldiers in the present war may lend valuable information on the above points. It is known now that the reaction from the sensitized vaccine inoculation is much milder, and immunity starts more rapidly. It remains for the future to decide whether or not this is more

lasting and to be used. The doses employed are similar to the non-sensitized, that is 500 millions, 1,000 millions and 1,000 millions at intervals of about seven days, or 1,000 millions and 2,000 millions at intervals of ten to twelve days. The inoculations are usually given subcutaneously.

Diagnosis of Typhoid and Paratyphoid by the Widal Reaction. A. Cade and E. Vaucher,⁷ from their extensive experience with typhoid and paratyphoid A and B, conclude that the Widal test taken methodically gives results agreeing with blood culture in the vast majority of cases. In two hundred and twenty positive blood cultures from both vaccinated and non-vaccinated cases, the serum reaction alone would have sufficed to place the cases in the typhoid groups in 90 per cent. Providing the serum was not taken too early in the disease, and neglecting agglutinations under 1/200 for the paratyphoids, and under 1/400 for typhoid, an exact diagnosis could have been made in 74.5 per cent. of the cases.

Regarding the behavior of the serum of those who have had antityphoid inoculation the authors state: "During the course of vaccination, the agglutinating power of the serum often obtains a high figure, 1/200, 1/500, 1/1,000 or more. These figures remain high for some weeks following and then rapidly fall, until at the end of three or four months the proportion is 1/10 or 1/50. There are, it is true, great individual variations in intensity and duration of agglutinating powers. Practically, one may say that in the majority of cases the agglutinating power will be very low or even *nil* five or six months after vaccination."

So that whether the patient has had a previous antityphoid vaccination or no makes no great difference in the Widal; the only precaution consists in disregarding typhoid agglutinations under 1/400.

The authors find the Widal test of especial value in those mild cases in which the blood cultures are negative, or in which the patient is seen too late for blood culture. It is of great importance to recognize the mild cases, as these may become foci of contagion.

Albuminuria as a Contraindication to Vaccination

(7) Presse méd., July 3, 1916.

Against Typhoid and Paratyphoid A and B. The effect of vaccination against these diseases in men with albuminuria of varying degree has been studied by F. Widal and H. Mery.⁸ A polyvalent vaccine was used. Men with severe nephritis were excluded, but men were vaccinated who presented 1 gm. or more of albumin to the liter of urine. No bad effects were evident in any case. The authors state that individuals with kidneys damaged too much to permit vaccination should not be accepted for active service. Under the influence of the vaccination the albumin content of the urine remained unmodified, dropped a little or showed a brief transient increase. In men with figured elements in the urine before the vaccination, these persisted unmodified afterward or showed a brief transient increase. Others in whom the urine had been free from them before showed transiently a few reds or whites or tube-casts afterward. The urea content of the blood and Ambard's co-efficient of urea excretion were determined in all the men with albuminuria. Occasionally the findings varied after the vaccination, but the fluctuations were minimal and transient. In a typical case the range was from 0.37 to 0.59, and back to 0.38 four days after the third injection, while the Ambard co-efficient dropped from 0.10 to 0.07. In others the range was downward. None of the vaccinated men showed any signs of renal insufficiency. Even those with pronounced Bright's disease manifested the same tolerance for the vaccinations.

Perforation in Typhoid and Paratyphoid in the Vaccinated. In 892 cases of typhoid and paratyphoid under the care of P. Guizetti⁹ in a hospital at Parma, during a five-month period, the mortality averaged 4.25 per cent. among unvaccinated individuals but was only 3.33 per cent. in those who had been vaccinated. Death was due to peritonitis from perforation in 44 per cent. of the fatal cases in the vaccinated and only in 12.5 per cent. of the unvaccinated. The perforation always occurred in the ileum, usually in the lower third. The author explains the greater frequency of fatal peri-

(8) *Presse méd.*, June 8, 1916.

(9) *Riforma med.*, March 31, 1917.

tonitis in the vaccinated by the statement that the vaccine moderated the symptoms to such an extent that the patients became careless. In one case the patient eluded the nurse and went to the latrine; the symptoms of perforation developed immediately afterward.

Disturbances in Individuals Vaccinated Against Typhoid. V. R. Stefansky¹ reports that out of every 400 or 500 men vaccinated against typhoid one at least would present considerable systemic disturbance. The temperature in these cases ran up to 102° or 104° F., with vomiting, diarrhea, jaundice, transient albuminuria and syncope. The symptoms disappeared in a day or two leaving no after-effects. Levy and Loeper have reported similar clinical experiences, and reproduced the disturbances in guinea-pigs after injection of a triple vaccine. Loeper ascribes the disturbances to a special affinity of the vaccine for the suprarenals, and combats it by injecting epinephrine to restore the blood pressure to normal. Stefansky thinks that the pathologic findings in the guinea-pigs' suprarenals are not convincing, as the suprarenals in these animals are damaged very easily by substances which do not injure human suprarenals. Stefansky reports an especially serious case of disturbances after injection of anti-streptococcus vaccine for chronic streptococcus affection. The first and second injections were without any ill effects, but a few hours after the third a serious condition developed suddenly, with cyanosis, almost imperceptible pulse, about 160, temperature 105° F. at times, with intense pain in the left flank, necessitating administration of morphine. This serious condition persisted for nearly three days and then subsided, except for the pains, which persisted for several days. These excessive reactions in his experience always occurred in persons who were apparently healthy. The intense neuralgic pains and vascular disturbances in his last case seem to point to bacterial anaphylaxis; there were no disturbances until after the injection had been repeated. He cites Kraus and Doerr's report that guinea-pigs injected subcutaneously with a small dose of typhoid, cholera or dysentery germs developed

(1) *Russkiy Vrach*, 1917, vol. 16, No. 3, p. 59.

typical anaphylaxis if three days later they were injected with a larger amount of the same. Stefansky thinks it probable that the disturbances after vaccination in man can be explained in the same way as the phenomena of anaphylaxis.

Suprarenal Reaction in Antityphoid Vaccination. Occasionally, says Maurice Loeper,² one sees after antityphoid vaccination a reaction consisting of marked weakness, headache, small, rapid pulse, pallor, increased respirations and other symptoms of cardiac weakness. Loeper shows that these disturbances are not of cardiac origin, since they are not relieved in the least by digitalis or camphorated oil, but are really due to adrenal insufficiency. This he shows also in two other ways: first by treating these patients with 0.5 mg. adrenaline, either by mouth or hypodermatically, the symptoms are at once relieved, and also by injecting antityphoid vaccine into guinea-pigs and demonstrating subcortical hemorrhages in the adrenal glands. Practically, therefore, one should estimate the arterial tension before giving the vaccine, and if this is found to be low to give a prophylactic dose of 1 mg. of adrenaline. Neither should the vaccine be given to one who is fatigued. Also, after the vaccine, if the pulse appears to be affected, a dose of adrenaline should be administered.

Differential Diagnosis. Stimulated by the reports from France of the large number of cases of typhoid fever which occurred among the soldiers early in the present war, C. J. Martin and W. G. D. Upjohn³ of the Royal Army Medical Corps made an intensive study of the large number of cases of enteric fever which were returned from the front between the months of October and December, 1915. One reason for this intensive study was to determine whether or not the illness diagnosed as enteric fever might not be largely paratyphoid rather than typhoid infection. Extensive detail as to the strength of serum which was necessary in order to produce agglutination of typhoid and paratyphoid A and B by the different patients is presented in this article.

(2) Presse méd., Oct. 19, 1916.

(3) Brit. Med. Jour., Sept. 2, 1916.

An analysis of the work shows that of 350 patients 6 were finally determined to be suffering from enteric fever, 25 (or 7 per cent.) had true typhoid, 213 (or 61 per cent.) paratyphoid A, and 112 (or 32 per cent.) paratyphoid B.

It was found, of course, that patients with paratyphoid A or B infection usually gave a positive Widal reaction with the *Bacillus typhosus*, because of the fact that most soldiers had been vaccinated against typhoid since the beginning of the war. This fact in conjunction with the large number of cases of paratyphoid fever led to the vaccination of British soldiers with the paratyphoid organisms as well as typhoid.

A study of the cause of some of the obscure cases of pyrexia among soldiers at the front has been made by A. H. Dirks, R. T. Thornley and R. A. Fawcett.⁴ They refer to the work of Professor Jacques Carles, who mentions three varieties of blood infection, which produces illnesses clinically distinguishable from paratyphoid fever. These three are caused by *M. tetragenus*, *Pneumococcus*, and *Bacillus coli*. Of these three types of infection, that of *M. tetragenus* is apparently the commonest, followed closely by pneumococcus infections.

Roughly speaking, the authors say, these disorders tend to fall into two general types: one resembles paratyphoid fever, and the other, in which the fever is intermittent, is spoken of as "trench fever."

The authors of the present article believe that a large proportion of cases of the illness known as trench fever are instances of one of these infections, and also those frequent cases of continuous pyrexia clinically resembling typhoid in which the presence of one of the typhoid group can be established.

They state that the *Micrococcus tetragenus* has hitherto been ignored as a pathogenic organism of importance; in a hundred consecutive cases of obscure pyrexia this organism has been isolated by the authors from the blood in pure culture on twenty-five occasions.

Mice when injected with this micrococcus die of septicemia, and the coccus has been regained from the heart's blood; further, healthy mice, when introduced

(4) Quart. Jour. Med., October, 1916-January, 1917.

to the cage of the septicemic mouse, have contracted the disease and died.

The detailed records of eleven patients who have suffered with this variety of infection are given in this article.

Clinically the *M. tetragenus* cases closely resemble one another. The onset may be sudden or insidious, the former being more common. Headache and pains in the lumbar region and down the legs from the knees to the ankle occur in nearly every case; tenderness over the tibia is sometimes extreme. Enlargement of the spleen and rose spots occurred in three of the cases. Anemia is common, and lethargy is the characteristic mental attitude.

Sometimes nothing but a slight headache is complained of and the patient runs a low form of pyrexia for a varying period—sometimes for a very long time. No fatal case occurred in the series here presented.

In a note on coccus infections it is stated that two other well-known cocci—the pneumococcus and the streptococcus—are also common causes of obscure pyrexia among men at the front. All these organisms are closely allied in their cultural characteristics, and all produce septicemia of the same sort of severity, though of different clinical types. The pneumococcus is apparently the cause of the intermittent fever which has been frequently described in the war zone. It also causes another type of illness in which abdominal pain, headache, and splenic enlargement, all occurring within the first day or two, are the characteristic symptoms. It may also produce fever less distinguishable from *M. tetragenus* septicemia. The streptococcus infection tends to be milder and more chronic, though in its severer forms it is hard to distinguish from the pneumococcus type. In all three fevers splenic enlargement is common. Mixed infections may occur. Probably four out of five cases of obscure pyrexia that the authors have seen in the war zone were due to one of these three infections. Tetragenus fever is the commonest and most characteristic, and presents the clinical appearance described.

[In civil and hospital practice, blood cultures in every case of pyrexia in which the diagnosis can not otherwise

readily be made, are a routine necessity. If they are habitually made, no chance for serious errors can occur. In civil practice, contrary to the statements here made, pneumococcus and streptococcus septicemias are always of grave prognostic import.—GEN. ED.]

History of Paratyphoid. Because of the amount that has been written about paratyphoid infections recently it has been thought well by Jay D. Whitman,⁵ captain in the Medical Corps, United States Army, to review the condition briefly. He refers first to the work of Eberth who, in 1880, isolated the *Bacillus typhosus* from the mesenteric glands and spleen of persons dead of this disease and so established its etiology beyond doubt. In 1896 Archard and Bensaude used the term "paratyphoid" as a name for organisms occupying an intermediate position between the *B. coli*; and the *B. typhosus* and capable of producing symptoms like those of typhoid fever. Schottmüller, in 1901, clearly demonstrated the two organisms, paratyphoid *A* and *B*, and showed their etiologic rôle in producing typhoidal conditions. The organisms have been named, therefore, the *B. paratyphosus A* and *B*, of Schottmüller.

They are exceedingly motile, even more so than the bacillus of Eberth. They have the same general morphology as typhoid organisms and the same staining reactions, but differ in their ability to produce gas in glucose-containing media. They are differentiated from the colon organisms in not coagulating milk, fermenting lactose or forming indol; paratyphoid *A* produces a *permanent* acidity in litmus whey, whereas paratyphoid *B* produces an acidity which is only *temporary*. The paratyphoid organisms are closely related to the Gaertner bacillus of meat poisoning, the *B. dysenteriae* of Shiga, the *B. icteroides*, and the bacillus of hog cholera. Group agglutination reactions are found among all three organisms, but in proper serum dilutions, specific agglutination reactions are present. Paratyphoid organisms are agglutinated by typhoid immune serum, but paratyphoid immune serum will not usually agglutinate the typhoid organisms. Typhoid bacilli are not very pathogenic for guinea-pigs and mice, but paratyphoid organisms are

(5) Military Surg., November, 1916.

extremely so, one-hundredth of a loopful of the *B. paratyphosus* causing death when injected intraperitoneally. Of the two paratyphoid organisms the *B* is much more common and widespread. It agglutinates more closely with the typhoid organism.

Infection with paratyphoid has been met with in all parts of the world. It never occurs as a great epidemic, as does typhoid, although it may co-exist with typhoid in endemic foci. In India, 15 per cent. of cases reported clinically as typhoid fever are found bacteriologically to be paratyphoid infections. Unquestionably a large percentage of paratyphoid infection is diagnosed and reported as typhoid fever, the disease being much more common than is generally supposed.

The disease is spread in much the same manner as typhoid fever. The symptomatology is classified as diarrheal or typhoid in form. The condition resembles closely food poisoning and disappears, as a rule, within from two to ten days. The typhoid form is more common and the following symptoms are said to occur in at least 20 per cent. of cases at the onset:

Headache, present in 85 per cent. of cases.

Diarrhea, present in 55 per cent. of cases.

General abdominal pain, present in 35 per cent. of cases.

Aching in the limbs, present in 30 per cent. of cases.

Mild intermittent shivering, present in 25 per cent. of cases.

Extreme general weakness, present in 25 per cent. of cases.

Backache, present in 25 per cent. of cases.

Epistaxis, present in 20 per cent. of cases.

Shivering and vomiting are more common in infection with paratyphoid *A* than with paratyphoid *B*. The temperature usually reaches its maximum in forty-eight hours. In 60 per cent. of cases there is a remittent type of fever, while in the remainder there is intermittent fever. The temperature seldom exceeds 103° F. The duration of the fever is from about fourteen to twenty-one days. The pulse is characteristically slow, slower even than in typhoid. A pulse of 70, with a temperature of 102.5° F., is significant of this type of infection. The

pulse is soft, sometimes dicrotic, and very easily compressible. It has been noted that when the pulse-rate does not exceed 100 in the first few days of the disease, the progress is extremely favorable. The blood-pressure is usually between 80 and 130 mm. Hg. Typical typhoid spots are present in from 60 to 75 per cent. of cases. They appear in crops, resembling in every way the rose spots of typhoid fever. The spleen is demonstrably enlarged in 80 per cent. and palpable in 35 per cent. of cases. Prostration, typhoid tongue and nervous symptoms are not usually so marked as in enteric fever, but may be present. Intestinal hemorrhage, perforation, appendicitis, cholecystitis, osteomyelitis, suppuration, adenitis, liver abscess and phlebitis have been reported, but are very rare.

The prognosis of paratyphoid fever is much more favorable than that of typhoid, the mortality of the former being given as 3.3 per cent., while that of the latter is from 9 to 25 per cent.

The treatment is practically the same as for typhoid, though the use of vaccines containing *B. paratyphosus* A and B as a prophylactic measure is generally recognized as a valuable procedure.

Much of the discussion in this paper is based on reports from the French and British armies in regard to conditions during the present war.

The following summary is presented:

The disease is more common than is generally supposed; many cases with typhoid symptoms, but negative Widal reaction, being paratyphoid fever.

Paratyphoid infections are extremely variable in their manifestations.

Carriers probably play the most important rôle in the transmission of the disease.

Endemics resembling food poisoning, due to paratyphoid bacilli, must be much more common than is generally supposed.

The "trench diarrhea" of Europe is an example. The disease, though usually mild, may cause extremely severe complications and death.

Considerable evidence has been submitted by competent observers to show that antityphoid vaccination does

not sufficiently protect against paratyphoid infections and that a polyvalent vaccine should be used, if such protection is necessary.

The fighting forces in Europe have suffered greatly from paratyphoid infections which, it is possible, might have been prevented had polyvalent vaccine been used.

Clinical Aspect of Paratyphoid. An extended consideration of the clinical aspects of paratyphoid fever are given by Charles Hewitt Miller¹ in two lectures delivered before the Royal College of Physicians in London.

The effects on the different anatomic structures of the body as summarized by this author are as follows:

Respiratory system: Rhinitis; pharyngitis; laryngitis; tracheitis and bronchitis; broncho-pneumonia and pneumonia; pleurisy—dry, serous, sero-fibrinous, purulent.

Alimentary system: Gastritis; enteritis and colitis with and without ulceration of the lymphatic tissue; appendicitis; inflammation of bile-ducts, gall-bladder and liver.

Urinary system. Nephritis; pyelitis and pyonephrosis; cystitis.

Skeletal system: Osteitis; synovitis, arthritis and peri-arthritis; myositis, myalgia.

Vascular system: Phlebitis; arteritis; possibly endocarditis, myocarditis and pericarditis; septicemia.

In addition, inflammation of the middle ear, iris, conjunctiva, meninges, testicle and epididymis have been seen.

Many of these anatomic lesions are more properly considered as complications, and for clinical purposes other forms of classification are more suitable.

The headings under which the author classifies paratyphoid infections are: (1) the typhoid; (2) the dysenteric; (3) the biliary—*i. e.*, jaundice and cholecystitis; (4) urinary—*i. e.*, nephritis, cystitis, etc.; (5) the rheumatic or arthritic; (6) the respiratory—*i. e.*, bronchitis, pneumonia and pleurisy; (7) the influenzal; (8) septicemic.

Under the typhoid type, in a general description he says that a period of incubation is difficult to calcu-

(1) *Lancet*, May 19 and May 26, 1917.

late. The onset is either gradual or sudden. Abdominal pain is recorded as one of the common symptoms. It is usually moderately severe and colicky and is not localized. Diarrhea occurs in more than half the cases. Nose bleeding occurs in about one-sixth. There is usually a very noisy cough with scant sputum. The temperature varies markedly. Some cases not exhibiting a temperature above 99° or 100° F. have been observed. The period of pyrexia is very short, or it may be of the classical typhoid type. Remissions of temperature may be pronounced all through the pyrexial period. The temperature may be of an irregular type.

The pulse behaves in a more orderly fashion than the temperature and is of importance in diagnosis both for its own characteristics and its relationship with the temperature. If the pulse is slow in relation to the temperature a definite diagnostic point is gained, and if with the symptoms pointing to enteric fever a relatively rapid pulse is found the prognosis is serious.

Concerning the rash, this author states that the commonest variety is the roseola, which is seen in true typhoid. A second kind consists of larger spots, of irregular outline, red with a blue tinge, raised, not fading completely on pressure, leaving a freckle-like mark of pigmentation after they have disappeared. The third variety is rare. Cyanotic subcuticular patches of irregular shapes and sizes are sometimes seen in severe cases. These patches may be the only evidence of a rash, or they may be mixed with other forms.

Sweating in paratyphoid is much more common than in true typhoid. Bronchitis occurs with great frequency during the first ten days. Cardiac inflammations are rare. The author has not seen a case of either pericarditis or endocarditis, but they have been recorded by other observers. A moderate degree of distension of the abdomen is almost always present. The spleen is enlarged in a majority of cases; it is palpable in half the cases and can be proved large by percussion in most of the others.

The liver edge is occasionally lower than normal, and deep tenderness over the area of the gall-bladder is fairly common. There is nearly always an initial diarrhea,

the stools being of liquid fecal matter. Under the heading of intestinal complications Miller says that hemorrhage occurs as in typhoid fever, but is not so frequent. Perforation is rare, but symptoms that cause perforation to be suspected are more common. Typical symptoms and signs of inflammation of the appendix are fairly common. Peritonitis without actual macroscopic perforation does occur, and may be localized or general; but it can not be distinguished from peritonitis due to perforation.

Other complications mentioned are: Furunculosis and subcutaneous abscess, suppurative and non-suppurative orchitis and epididymitis, splenic and hepatic abscesses, abscess of the brain, osteitis, periostitis and abscess of bone. Of the bones of the body the ribs and tibiae have been affected more commonly.

Thrombosis of different arteries, most frequently arteries of small size, has been recorded.

The relapses in paratyphoid occur in different percentages according to the different observers. The progress of the convalescence in paratyphoid is slow; normal vigor does not return; the patient constantly says that he feels weak and "good for nothing." Lassitude, a morning headache, lack of appetite, inability to sleep in the early part of the night and waking up unrefreshed are frequent complaints. This is a very different picture from the convalescence of typhoid fever.

Among the nervous disturbances mentioned are spasmodic asthma, paroxysmal headache and melancholia.

Miller says that the term dysentery should be limited clinically to those cases in which there is a frequency of blood and mucus accompanied by pains and tenesmus. In regard to the question as to whether or not the paratyphoid organism can cause dysentery, he refers to post-mortem results furnished by Lieutenant G. B. Bartlett, who studied mixed infections of amebiasis and paratyphoid. His cases are said to demonstrate that amebic ulceration of the colon may be present without any symptoms of dysentery. It was discovered post-mortem in a patient who died from enteric fever due to *B. paratyphosus B*, in whom there had been no symptoms of dysentery. Signs of amebic dysentery may begin in the

stage of convalescence after paratyphoid fever. Patients may be admitted to hospitals suffering from amebic dysentery and may develop paratyphoid fever in addition to the amebiasis.

Concerning the biliary attack of paratyphoid fever Miller says that according to some observers infection of the gall-passages and gall-bladder in this disease have been very frequent, while according to others it has been rare. Among the cases of the author's series, a jaundice of the catarrhal type has been seen as follows:

1. Quite early in the illness; more often it appears after a period of malaise. It resembles a simple catarrhal jaundice in character and is seldom severe or troublesome.

2. It can appear later in the illness; it has been seen on several occasions during the unsatisfactory stage of convalescence when the temperature is not steady. It is of the catarrhal type in these cases, but is rather more severe and lasting in the latter.

3. It has a tendency to become recurrent. After the patient has had a mild attack of jaundice, has quite recovered and been in good health for months, jaundice may return and be much more severe than in the original attack.

Miller thinks that there is no doubt that the paratyphoid organisms frequently invade the biliary system, but do not so frequently cause jaundice at the time; there is, however, considerable danger of chronic cholecystitis with the formation of gall-stones months or years afterward. There is great danger that the gall-bladder may become a reservoir of infected bile that will be periodically discharged into the intestines.

When in the course of paratyphoid fever the urinary tract is involved albuminuria is commonly present for a few days at the height of the fever, but this hardly needs comment. There is a great tendency for the paratyphoid organisms to find their way into the urinary tract and occasionally they can be found in the urine, both in the acute stage and afterward, for a varying length of time without any evidence of infection of the urinary tract. Acute nephritis is fairly common; it

was present in 4 per cent. of the cases considered in these lectures.

Under the rheumatic type of paratyphoid fever Miller includes those cases in which there is acute articular rheumatism, or a condition more closely resembling the "infective" type of arthritis. The latter is the more common of the two.

Another variety was observed, and for want of a better term the author calls this the "trench fever type." Before there were such complete and detailed accounts of trench fever, he noted that occasionally painful, tender shins, worse at night, were symptoms of a mild type of paratyphoid fever. The onset in these cases was sudden, the temperature was usually not so high as 103° F.

Associated conditions that he mentions are: Bronchitis, pleurisy and lobar and bronchopneumonia, which were seen at fairly frequent intervals. Influenza and paratyphoid fever have much in common he says; not only do both diseases appear in divers forms, but paratyphoid fever can imitate the forms of influenza so closely that at the onset of the fever it may be impossible to distinguish between the two conditions. Later in the course of paratyphoid it may be expected to find some of the signs that point to an enteric infection, but they do not always appear, and the diagnosis is made by the bacteriologist on nothing more than the suspicions of the clinician.

The Paratyphoid Carrier. In the Goulstonian Lecture, delivered before the Royal College of Physicians of London, C. H. Miller² after discussing the disease very extensively says of carriers:

"But however numerous are the possible intermediate agents in spreading paratyphoid infection, it has to be remembered that the real cause of infection is the infected human being. In the acute stage of paratyphoid fever precautions are taken to limit the possibilities of dissemination. In the case of the carrier the danger is greater, because it may not be suspected. A carrier may be an individual in perfect health who can mix freely with his fellows. In communities where there is good sanitation and water

(2) *Lancet*, June 16, 1917.

drainage the dangers of the carrier are lessened. But even in these circumstances epidemics have been traced to an unsuspected carrier. In barracks, camps, and billets the danger from a carrier is greatly increased, and measures have to be taken to prevent the possibility of the contamination of food and water and to protect the individual by raising his resistance to the infection.

“The carrier is usually an individual who has had a recognizable attack of enteric fever, but some of the cases are so mild that they are not suspected. These mild cases are the most dangerous from the point of view of the sanitary officer, and they are probably becoming more numerous. Carriers are of different sorts. The majority are those individuals who pass the organisms in their stools. The gall-bladder is commonly a nest for enteric organisms, and there may be periodical discharges of enteric-laden bile into the intestine. Some of these ‘gall-bladder’ carriers have chronic cholecystitis, and they may have recurrent symptoms which may call attention to the nature of their condition. The most dangerous carrier of all is the male urinary carrier. The fecal carrier may be expected to pass his infective material into a proper latrine whenever it is possible; the urinary carrier will have a much wider range of action.

“The carrier is not only dangerous to others, but he is living in danger to himself. At any time he may develop acute symptoms of paratyphoid fever. It only needs some lowering of resistance by fatigue, shock, wounds, gassing, and even inoculation against an infection for the autoinfection to become severe. Such considerations make it impossible to calculate the incubation period of the disease from observations made on troops in the field.

“There does not seem to be any time limit for the carrier. In the case of cholecystitis quoted above the patient had contracted his original infection sixteen years before, and I have heard of a similar case with a fifty years’ interval.

“It is difficult to be certain that a patient who has recently had paratyphoid fever is free from infection.

Thus one convalescent who remained in hospital for the treatment of other conditions had one positive stool on October 7 and another on February 7; there had been six negative examinations in the interval. On another occasion, during a spell of hot weather, nearly all the convalescents whose stools had been negative for some time had a positive result.

"It is obvious that the carrier is one of the most difficult problems of military hygiene. It is certain that when organisms are found in the excreta a patient is dangerous and must be segregated. But when they are not found, even over a long period, it is not certain that the man is free from infection. Prolonged segregation and repeated examinations are the only measures that can be taken, and they do not give absolute security."

In conclusion, Miller says that in the campaign against paratyphoid infection we must aim at personal hygiene, good sanitation, preventive inoculation, segregation of carriers, and, on the part of the clinician, early diagnosis.

Paratyphoid Fever in the American Army. A description of camp conditions which are thought to have been responsible for an epidemic of paratyphoid fever among soldiers from New York State, camped on the Mexican border during the summer of 1916, and an account of the disease as observed in these soldiers is presented by Charles White Berry³ of Brooklyn, N. Y.

When the soldiers had returned to New York and figures were obtained, it was found that seventy-four physically well men were carriers of *B. paratyphosus*, and 137 were either acutely ill or convalescent from the disease, all of them having had positive results from stool examination. This gave a morbidity of 211 positive cases of paratyphoid fever among 1,000 men when the regiment returned from border duty, and does not include the mild and overlooked cases, nor those men who had been inspected and returned to the command before the regiment was ordered home. Had these cases been included, the total would have been nearly 300 cases, or about 33.3 per cent. of the entire command.

(3) Med. Record, Jan. 27, 1917.

It was found by subsequent examination of stools that the carrier state did not tend to persist, but under the influence of more healthful living and surroundings, infection seemed to die out in most cases. In some men, however, positive results were obtained after several examinations at intervals of from one to four weeks.

In discussing the symptoms Berry states that muscular pain was often the first symptom noted by the patient. All stages of severity were seen, one patient requiring morphine for the severe backache. The pains were usually a general soreness over the entire body, like that described in grippe infection; in other cases the pain was more prominent in the back of the neck, lumbar region and legs. Insomnia was noted in some of these patients and epistaxis in a very few. The gastro-enteric system did not seem to be much in evidence in the most acute infections.

Constipation often alternated with diarrhea. An eruption appeared in about 50 per cent. of the cases, being noticed from the seventh to the fourteenth day. It was similar to that of typhoid, appeared in crops usually in the umbilical region, ten spots being the greatest number seen at one time.

Rapid emaciation and muscular weakness were seen in all of the cases. Abdominal distention was noted in a few cases, but was not a prominent feature. Intestinal hemorrhage was not seen. Delirium, or so-called "typhoid-state," was rarely seen. Some of the patients with temperatures of 106° F. would readily enter into conversation when spoken to.

The duration of the disease was from two to six weeks. In the shorter cases it was not unusual for a relapse to occur, and the patient again to take to his bed after he had apparently recovered. The second illness lasted as long or longer than the original attack. This part of the clinical picture resembled to some extent attacks of relapsing fever.

It was noted that healthy carriers would often go on for a long time apparently well, and then suddenly come down with the disease a second time.

The prognosis as judged from this experience is good, since, in all these cases, not one death was encountered.

The treatment of paratyphoid *A* is recommended as that of acute gastro-enteritis, and that of paratyphoid *B* the same as typhoid fever.

An Epidemic of Jaundice in a Concentration Camp Due to Paratyphoid Bacillus "B." Frugoni and Camata⁴ observed among the troops operating in the valley of Judrio a hundred or so cases of jaundice, with a clinical evolution like catarrhal jaundice secondary to gastro-intestinal catarrh, but having some features recalling the infectious pseudo-catarrhal jaundice of Chauffard's type.

The jaundice was sometimes seen alone, but generally it was preceded by a diarrhea with the features of a gastro-intestinal catarrh. There were clayey stools in 54 per cent. of the cases. The liver was enlarged, sometimes markedly. In 60 per cent. of the cases the spleen was enlarged. In 25 per cent. there was a brief initial fever. Bradycardia was present in 52 per cent. Investigation for hemorrhagic diathesis was negative. The course of the disease was benign, without complications or relapses.

To get at the pathogenesis, bacterial examinations were made on the bile obtained by duodenal catheterization according to Einhorn's method. Results were negative for vibrios, *Streptococcus hemolyticus*, and Pfeiffer's bacillus. In one case, Eberth's bacillus was isolated and in 25 per cent. of the cases *B. paratyphosus B*. This last was isolated in pure culture three times from the stools. Blood culture was always negative.

Seroreactions were positive for agglutination at a dilution of 1/100 (and once 1/200) for *B. paratyphosus B* in patients from whose bile the organism was isolated and even in some others whose bile was negative, but in these latter agglutination was very feeble.

The authors conclude that most of the cases in this epidemic were due to *B. paratyphosus B* of slight virulence, which under favorable conditions lodged in the biliary tract and from this single focus gave as the important clinical symptom, jaundice and also the reaction of the organs (enlargement of the spleen) and reaction of the blood (agglutination).

(4) Presse m.d., Dec. 18, 1916.

[Interesting in this connection is the history of early outbreaks of so-called epidemic catarrhal icterus described in medical literature and figuring in text-books. It is likely that all such forms were general infections, with local effects upon the gall-bladder and biliary passages, or that they were cases of paratyphoid, then unknown.—GEN. ED.]

Experimental Gall-Bladder Infections with Typhoid, Cholera and Dysentery. With an ultimate view of studying typhoid carriers and the rôle played by gall-bladder infections in this connection, Henry J. Nichols,⁵ major, Medical Corps, United States Army, has made a series of experiments in which rabbits and guinea-pigs were inoculated with live strains of typhoid, paratyphoid A and B, cholera vibrios, and dysentery bacilli. The work is chiefly concerned, however, with the typhoid and paratyphoid organisms. Injections were made into the ear veins and mesenteric veins of animals in which there had been produced fistulas of the common bile duct. The bile was collected at stated intervals following injections of live bacteria, and cultures were made to determine whether or not any of the organisms were excreted through the bile and what, if any, relation could be established between the size of the dose injected and the number of microorganisms that appeared in the bile. The antiseptic effect, *in vivo*, of bile from man and certain animals on different organisms was also studied. Animals that had been immunized by injections of small doses of typhoid and paratyphoid bacilli were tested for their ability to eliminate the live organisms that were later injected in large doses.

Concerning the mechanism of gall-bladder infections in typhoid, Nichols states that logically the lesion might be due to descending infection of the bile from the liver; to an ascending infection of bile from the intestines; or to a transverse infection through the gall-bladder wall from the blood-vessels. A review of the literature on this point leads the author to believe that the first-named route of infection is the most likely one, and this opinion is supported by his own experiments. Bacilli were found in the bile following injections into the

(5) Jour. Exp. Med., November, 1916.

blood-stream; more bacilli were found following the injection of larger doses, and more were found following mesenteric vein injection than ear vein injection; also more bacilli appeared in the bile of immunized animals than in that of the non-immunized. This last condition is explained on the ground of rapid agglutination *in vivo*, deposition of bacilli in the liver, and corresponding elimination. Gall-bladder infections in immunized animals are, therefore, not necessarily an index of lack of immunity, but may, in part, be an indication of a rich amount of immune bodies in the blood.

The antiseptic action of bile was tested by placing one loopful of a broth culture of different organisms in 1 c.c. of different kinds of bile. One loopful was plated immediately and one after twenty-four hours. The results are shown in the accompanying tables.

ANTISEPTIC ACTION OF BILE.

1 loop plated immediately.

Bile.	Typhoid.	Para-A.	Para-B.	Chol. era. (Flexner).	Dysentery	Colon.
Ox	240	320	180	10	160	640
Human	1,000	1,600	1,600	50	400	1,600
Rabbit	400	500	800	40	500	In.*
Guinea-pig..	400	400	500	5	640	800

*In. indicates innumerable.

1 loop plated after 24 hours' incubation.

Bile.	Typhoid.	Para-A.	Para-B.	Chol. era. (Flexner).	Dysentery	Colon.
Ox	In.	In.	In.	In.	In.	In.
Human	"	"	"	"	"	"
Rabbit	—	—	—	—	—	—
Guinea-pig..	—	—	—	—	—	—

The antiseptic action of rabbit and guinea-pig bile is accounted for by the high alkalinity, and this suggests that giving alkalies to typhoid convalescents, or carriers, might produce a sufficient degree of alkalinity to destroy whatever infection of the gall-tract had taken place. The statement is made that it is apparently possible to protect the rabbit to some degree against gall-bladder infections by a previous injection of sodium bicarbonate.

Diagnosis and Treatment of Typhoid Carriers. In the preceding article Henry J. Nichols, major, Medical Corps,

United States Army, called attention to the problem of the pathogenesis of gall-bladder lesions in typhoid and allied diseases, and emphasized the mechanism of descending infection of the bile from the liver. He showed by means of the common duct fistula method in rabbits that more typhoid bacilli appear in the bile with larger intravenous doses; that more bacilli appear after mesenteric than after ear vein injections; that more bacilli appear in immunized animals than in normal animals, and that more actual gall-bladder infections occur under these conditions, which favor the presence of micro-organisms in the bile, than otherwise.

The mechanism of infection in the case of typhoid, cholera and dysentery organisms seems, therefore, to be different from that in case of streptococci which, as has recently been shown by Rosenow, seem to infect first the gall-bladder wall by means of emboli.

The various new mediums which are still being devised for the detection of typhoid bacilli in the feces show that this method is not altogether satisfactory, and a concrete example is found in the fact brought out by Garbat's⁷ cases, and also by the author, that the duodenal contents of early carriers may contain typhoid and paratyphoid bacilli while repeated examination of the feces fails to reveal them.

The technique used for the detection of typhoid bacilli in the duodenal contents in the present work⁸ was as follows:

"A regular breakfast is allowed at 7 o'clock; in about two hours the metallic sinker is chilled in ice water and is put in the mouth with the patient sitting up in bed, and a small drink of water is given; as soon as the patient swallows the sinker he lies down on the right side and waits for the tube to descend to the duodenum (third mark). On an average, a wait of about four or five hours was necessary. At the end of three hours the tube is primed by aspiration with a syringe, which usually produces a small amount of whitish mucus, acid to litmus. This procedure often establishes a siphon, and in another hour yellowish-

(7) Page 64, this volume.

(8) Jour. Amer. Med. Ass'n., March 31, 1917.

green fluid, neutral or alkaline to litmus, may be dropping out of the tube. Further suction gives from 10 to 20 c.c. of genuine duodenal contents. If the contents are still acid, a further wait is necessary, and rarely another trial on another day must be made. No special hardship is involved, and one patient took the tube four times. Altogether twenty-eight successful attempts were made out of thirty-two trials on twenty-five patients. Endo plates are inoculated as soon as possible, one with the straight fluid and one with the centrifugate. Another portion is put in brilliant green peptone water, 1:20,000, and plated on Endo's medium after twenty-four hours' incubation."

In the duodenal contents of two of the twenty-five patients examined in this way, organisms were found; in one paratyphoid A, and in the other typhoid bacilli. Each of these patients was given 2 gm. of sodium bicarbonate three times a day for ten days, following which repeated examinations of the duodenal contents and feces failed to reveal the bacilli.

"The superiority of examination of duodenal contents over that of the feces for the detection of carriers is, of course, to be expected theoretically and seems to be strongly indicated by the few cases so far examined. Whether the bacilli are constantly or only intermittently present in the duodenal contents of a carrier will have to be determined by further work; the chances favor the former possibility; but if bacilli are only intermittently discharged, the gall-bladder may be stimulated to contract during the examination by a preliminary meal, as suggested by Garbat.

"The number of permanent carriers of typhoid bacilli is usually put at about 3 per cent. of cases, while temporary carriers run much higher, depending on the time of examination. Examination of the duodenal contents may increase the percentages for both kinds of carriers, but especially for temporary carriers. In this connection a practical point is the proper time after recovery for examination, because the bile always contains typhoid group bacilli at some period of the disease. Probably at least a month should pass after the temperature is normal before the test is made, in order

to avoid picking up the purely temporary carriers which clear up of themselves."

Bacteriologic Examination of the Duodenal Contents in Typhoid Convalescence. This subject has been studied by A. L. Garbat.⁸

The object of the work was to substitute for stool examination a more simple and more accurate means of determining when an individual is a typhoid carrier. It would be unfair to refer to this work without quoting the following statement regarding statistics on typhoid fever:

"Of every 10,000 apparently perfectly healthy residents, 2.3 are typhoid carriers. Fifty-five per cent. of all typhoid cases are due to carriers either directly or indirectly; 17 per cent. are due to direct contact with carriers; in exact numbers, Gaetgens found that out of 386 cases, seventy-seven, or 20 per cent., could be traced to chronic typhoid carriers.

"Park has estimated that one in every 500 adults who never knowingly had typhoid is a typhoid carrier.

"Of every hundred typhoid patients, from three to six become typhoid carriers.

"Naturally, it must be remembered that typhoid carriers may be either permanent or temporary. Thus one can apply the expression *omnis typhus ex typho*. The ideal of prophylaxis in typhoid is therefore detection of typhoid carriers. It should be the duty of hospitals and physicians taking care of typhoid patients to be certain on discharging their patients that the latter are not typhoid carriers. The usual way of determining this, when it is done at all, is by examination of urine and stool. The examination of the urine for typhoid bacilli is simple, the disadvantage being that as a general rule only a small percentage of cases continue to show typhoid bacilluria; usually the excretion of the bacteria is by the feces.

"The examination of the feces is under ordinary circumstances attended with marked difficulty. The overgrowth by colon and other bacteria makes it necessary to have special media, of which great numbers have been

(8) Jour. Amer. Med. Ass'n., Nov. 18, 1916.

devised, but even then success is difficult and not assured."

It has been determined by specific inquiry that a large number or a high percentage of hospitals in this country do not make appropriate bacteriologic examinations of the excreta of convalescent typhoids before discharging them, in order to determine whether typhoid carriers are dismissed or not.

Considering the gall-bladder or bile as a source of entry of the bacteria of typhoid bacilli into the intestines, numerous observers have attempted in various ways to get large collections of bile for bacteriologic examination. The methods used, however, have not been particularly successful. The procedure used by Garbat consisted of passing a duodenal tube, the Einhorn variety, before the patient retired at night. On the following morning he received a fluid breakfast to assure the passage of the tube into the duodenum and stimulate the secretion of bile. About one and one-half hours afterward the tube and duodenum were washed out with sterile water or saline solution by injecting from 8 to 10 oz. of sterile water or saline through the tube and in half an hour to an hour aspirating with a sterile syringe. In this way large quantities, in some instances as much as 28 or 30 c.c., of pure, clear bile were obtained.

Of twelve patients examined in this manner the bile from two were found to contain typhoid bacilli, and in each of these two the urine and stool cultures were negative culturally.

Since it is well known that typhoid infections of the urinary type may exist when no typhoid bacilli are present in the gastro-intestinal canal, it is necessary with such bacteriologic examination as this to examine the urine also. The aim of this work is simply to replace the stool examination by the much simpler and apparently more accurate examination of the bile.

High Caloric Feeding in Typhoid Fever. In speaking of the experience in the wards of the Brooklyn Hospital with high caloric feeding in the treatment of typhoid fever during the last three years, Dudley Roberts⁹ states that three points have been established:

(9) New York Med. Jour., Jan. 27, 1917.

First, that the results of this method of treatment are marvelously good; second, that it is practicable in almost every case to administer the high caloric diet; third, that with definite formulas of known value to the ounce measure, it is possible to administer the desired caloric intake and to know, from hour to hour, and from day to day, just how much is being ingested, even though the nurse or attendant is comparatively inexperienced in such matters.

A history of the dietary management of typhoid fever from the time when patients were practically starved to the present is given. The report of the author's own work is based upon the management of seventy-two patients suffering with typhoid and given the high caloric diet. Five, or 5.5 per cent., of these individuals died and it is stated that the dietary management in these instances was not carried out so completely as it was with the others of the series. The deaths all occurred early in the series and in each instance there was some severe complication.

Roberts states that the diet was given on the basis of a feeding every two hours, starting at 7:00 in the morning. The amount and kind of each feeding is charted, the calories being read from a table supplied to the nurse, a copy of which is shown in the accompanying table. The selection of the various formulas for different feedings is left to the nurse, who suits, as far as possible, the desires of the patient. A sample of the feedings for a day is shown in the second table. From this it is seen how easy it would be to increase the number of calories each day and still maintain a good selection of food. As a general rule it has been found that the strong adult male does well on from 4,000 to 4,500 calories, women and children on about 1,000 less. Many children crave more than this, and it is said that no ill effects have been encountered by satisfying their appetites.

The presence of tympanites in the patient is not considered an indication for reducing the diet. When visible blood appears in the stools there has been some reduction in the amount of food, but little or no change in the quality.

(FOOD FORMULAS FOR HIGH CALORIC FEEDING.)

Food Formulas	Amount	Carbohydrate in grams	Fat in grams	Protein in grams	Calories	Calories per ounce	Ways of Serving
1. Milk	2 oz.	12	9.5	2.4	160	20	Hot or cold, or as junket
2. Milk	6 oz.	9	6.5	6	120	20	Hot or cold
3. Cream (40%) ..	2 oz.	1.8	24	1.5	240	45	Flavored with tea or coffee or cocoa
4. Milk	6 oz.	9	6.5	6	120	20	As junket
5. Cream	2 oz.	1.8	24	1.5	240	45	As hot drink
6. Lactose	1 oz.	30	6.5	6	120	20	Flavored with tea or coffee or cocoa
7. Cream	2 oz.	9	6.5	6	120	20	Flavored with vegetable or meat as soup.
8. Lactose	1 oz.	30	2.4	1.5	120	20	Flavored with vanilla or chocolate
9. Egg	one	12	3	7	80	12	To be used as food drink with brandy or whiskey
10. Orange juice ..	4 oz.	12	2.4	1.5	120	20	Cooked as custard or made into ice cream (sweetened)
11. Egg	1	12	2.4	1.5	120	20	As hot soup flavored as above
12. Lactose	1 oz.	30	2.4	1.5	120	20	Preferably ice cold
13. Vichy or water ..	4 oz.	12	2.4	1.5	120	20	Serve as food drink or frozen as water ices
14. Cereal (cooked) ..	5 oz.	12	2.4	1.5	120	20	
15. Cream	2 oz.	9	6.5	6	120	20	
16. Lactose	1 oz.	30	2.4	1.5	120	20	
17. Cane Sugar	1/4 oz.	25	3	5	120	65	Slice 4"x4"x1/2" thick=50 gm.
18. Bread or toast ..	50 gm.	25	3	5	120	65	Add steaming milk as desired
19. Milk toast	50 gm.	25	3	5	120	65	
20. Cream	2 oz.	9	6.5	6	120	20	
21. Lactose	1 oz.	30	2.4	1.5	120	20	
22. Butter	10 gm.	18	8	7	65	1" cube	Sugar to taste
23. Baked apple ..	1	18	8	7	65	1" cube	Sugar to taste
24. Lactose	1 oz.	30	2.4	1.5	120	20	Flavored with beef, wine or fruit
25. Cream	1 oz.	9	6.5	6	120	20	
26. Jelly	1 oz.	9	6.5	6	120	20	
27. Gelatine q. s.	1 oz.	30	2.4	1.5	120	20	
28. Lactose	1 oz.	30	2.4	1.5	120	20	
29. Cane sugar	1 dr.	8	1.5	1.5	15	50	
30. Water q. s. ad.	5 oz.	9	1.5	1.5	15	50	
31. Cream (whipped) ..	1 oz.	9	1.5	1.5	15	50	
32. Potato (medium) ..	3 oz.	35	8	3.5	90	65	
33. Butter (inch) ..	10	70	12-20	12-20	120	120	Each kind must be weighed in fractions of oz.
34. Crackers	3-10	70	12-20	12-20	120	120	

Roberts says that the results obtained by this plan of management are excellent, changing the usual picture of typhoid to such an extent that the disease is hardly recognized, clinically, as the old enteric fever.

CHART OF ONE DAY'S FEEDINGS.

Hour.	Formulas.	Amount.	Calories.	Totals.
8 a. m.	Nos. 7 and 3	4 and 3 oz.	460
10 a. m.	No. 4	6 oz.	420	880
12 m.	No. 9		545	1,425
2 p. m.	No. 11	6 oz.	300	1,725
4 p. m.	No. 4	5 oz.	350	2,075
6 p. m.	No. 3	6 oz.	360	2,435
8 p. m.	Nos. 7 and 3	4 and 3 oz.	460	2,895
1 a. m.	No. 6	6 oz.	180	3,075

The Reflexes in Typhoid Fever. In an account of his observations on this point, E. B. Gunson,¹ of the British Army Medical Corps, states that when the quadriceps femoris muscle mass is firmly grasped just above the knee, between the thumb and fingers the patient experiences considerable pain referred to the site of stimulation, and there occur flexion at the hip-joint and extension of the great toe of the opposite limb. The reflex may be incomplete and consist of flexion at the hip only or of flexion at the hip and contraction of the tensor faciae femoris muscle without actual extension of the great toe; crossed extension of the great toe without flexion at the hip occurs in some cases. Pain on stimulation is a marked feature, and usually persists for several days after the reflex movements can no longer be elicited. Similar, but uncrossed, movements of the limb which is stimulated may also occur. This condition was observed in a fairly high percentage of the small series of cases studied by Gunson, and in several hundred patients studied by his colleague, J. W. C. Gunn. In patients who presented this change in reflex, the knee-jerk was frequently absent. Babinski's sign was present in one positive and in two of the negative cases. Ankle-clonus was not met with. The abdominal reflexes were absent or greatly enfeebled in many of the cases which presented the cross reflex, but in more which did not present the latter. The presence of the cross reflex in enteric fever is held to signify a "temporary perturbation" of the spinal cord, the result of a toxic or inflammatory process, on which some of the other reflex

(1) Lancet, Sept. 16, 1916.

changes may also depend and to which the extreme weakness of the limb and back muscles may in part be attributed. The reflex was found to be of some diagnostic value, as it was never present in doubtful cases which on subsequent bacteriologic examination proved to be simple enteritis.

The Location of Myositis in Typhoid and Paratyphoid. According to P. A. Daudon,² acute suppurative myositis occurring in the course of or during convalescence from the typhoid state has never been made a subject of statistics, but occurs at least in 1 per cent.

Tendency to localization is noticed, especially during convalescence, but may occur in the acute typhoid state. It seems to be independent of the intensity of the general infection.

Acute localized myositis, due to colonization of bacteria in a muscle or in groups of muscles is easily diagnosed from the general diffuse muscular changes so commonly seen and which are of a toxic nature.

Myositis most commonly occurs in those muscles used the most during the disease, namely: the abdominal muscles, triceps, brachial and calf muscles and, commonest of all, the shoulder muscles. Localization in the pectoral group is likewise common and classical.

The relative frequency in typhoid and paratyphoid is not known, since these diseases have only lately been separated.

In paratyphoid conditions the number of observations are very few. One concerned a hematoma of the abdominal muscles. Another focus was in the right pectoral muscles and went on to suppuration; a culture of paratyphoid A was obtained from it.

The treatment of typhoid myositis is the ordinary treatment of inflammation.

Institution Typhoid Combated by Vaccination. An outbreak of typhoid fever in an insane asylum is reported by P. B. Newcomb,³ of Mount Pleasant, Iowa.

During the late summer of 1915, the town of Osawatomie, situated one mile from the hospital, suffered an epidemic of typhoid fever comprising

(2) Presse méd., Dec. 18, 1916.

(3) Jour. Amer. Med. Ass'n., Dec. 9, 1916.

twenty-five cases. At that time no cases appeared in the hospital. During November and December of the same year, four typical cases developed in the institution. In addition to these were several atypical cases, and one of these patients, F. J., was confined to his bed but a few days. His was the first suspicious case seen at the hospital.

In January and February, 1916, other suggestive cases of illness occurred which conformed neither to the ordinary conception of influenza, which was then rampant over that section of the country, nor to typical typhoid fever, and no positive Widal reactions were obtained. At this time, however, the patient F. J. gave a positive Widal reaction. The feces and urine were examined and no typhoid bacilli found in any case.

From early autumn Newcomb had urged the advisability of immunizing the attendants and patients, but the procedure was unfortunately not inaugurated until an epidemic had manifested itself. The disease can be said to have been endemic in the hospital from November until March, when an epidemic occurred, the latter consisting of forty-one well defined cases.

During the latter part of March, a number of the officers and employees voluntarily subjected themselves to typhoid vaccination. April 5, twenty-one persons had been stricken, among whom was the superintendent of the institution. There was imminent danger of a very extensive and disastrous spread of the infection. Authority was obtained from the board of control to enforce general immunization on officers, employees, families resident on the grounds and patients alike. Very few objections were raised to this arbitrary order, and no refusals, resignations or dismissals occurred in consequence. Inoculation was begun the day after the order was issued. The bacterin used at this time was the ordinary serial package from a reliable pharmaceutical house. It was foreseen that the amount of bacterin which would be required for complete immunization for the entire hospital population, if furnished at the market price, would be almost prohibitive. A quantity of bulk bacterin was therefore prepared from

the same strain of bacillus as that used by the army. The suspension was made so that 0.5 c.c. contained one-half or one billion bacilli as required for the initial and two subsequent doses. About 150 doses of the commercial bacterin were given, and the remaining 4,378 doses were from the bulk laboratory preparation.

All inoculations were made at night. Patients of the better class and those of a chronic demented type were ranged in line on their ward corridors. This arrangement saved much time, and was far more convenient than going from room to room. Nurses had the patients' arms bared, and the assistant, preceding the physician, applied iodine at the insertion of the deltoid. With resistive patients and those in seclusion, the application of iodine and the subsequent injection were made at the most accessible part, usually the leg or thigh. No abscesses followed the injections. The average time required for inoculation was twelve seconds per subject among the acute, and eight seconds among the chronic patients.

No severe reactions were noted, although a few patients experienced mild chills. Agglutination tests following immunization have not been made.

Every effort was made to locate the source of the infection. Carriers were looked for, but none found. The food supply came from ten different sources. The water supply for all buildings was the same, a drilled well, 165 feet deep. Water from this well was held in high repute in the hospital community because repeated analyses failed to show any contamination. Suspicion was directed toward this well because of its proximity to an unlined reservoir which was supplied from the Marais des Cygnes River, a stream which overflows its banks with every heavy rain and which is little less than a drainage ditch for several counties. This reservoir was about 100 feet from the well. The water in it was used for washing. Water from the well was drunk by the officers and patients, but it was impossible to prevent some of the patients from drinking the reservoir water direct from the taps in the toilet rooms. Among the latter there was practically no typhoid fever.

It was necessary to direct attention in another direction. It was found that a kitchen drain from Cottage B ran within about 15 feet of the well. On suspicion the well was accordingly closed, April 10, the day on which the location of the drain was found. Thereafter all water used in the hospital was boiled river water.

Exhumation showed the drain to be an open-joint earthen pipe laid many years before, and honeycombed with leaks. The drain was crossed above by a sewer of poor construction which also drained a portion of Cottage B. Near the intersection was found an area of seepage from the sewer above to the kitchen drain beneath at a point where it ran nearest the well and toward it. No area of seepage was found from the reservoir mentioned above and the well. It is interesting to note that the employee F. J., the first suspicious case to appear at the hospital, was cook at Cottage B., where he resided. He had visited the town of Osawatomie frequently during the time that typhoid fever was epidemic there. The patient who was the first case in the acute outbreak at the hospital was an inmate of Cottage B. Examination of the well water showed the presence of *Bacillus coli*. No typhoid bacilli were found.

In commenting on this outbreak Newcomb says that the preferable way of dealing with institutional typhoid epidemics is to prevent their occurrence by means of a general immunization whenever typhoid is in the vicinity, or on the advent of the first suspicious resident case.

Routine inoculation of new patients and recently installed employees at stated intervals would conduce toward safety, and should be made the rule in any institution with a large resident population. This routine inoculation with bacterins can be made compulsory without serious objection on the part of patients or employees, and can be carried out speedily, effectively and with perfect safety.

It is impossible to determine absolutely whether the checking of the epidemic mentioned was entirely due to the use of typhoid vaccine or to the closure of the suspected well. From the recorded experience of

others in the use of typical vaccines, and from the facts here reported, however, one is inclined to believe that the vaccine played at least a very important part in the control of the epidemic.

In any epidemic, all sources of food and water supply should be under suspicion and examined most carefully, no matter what their previous reputation may have been.

Typhoid Outbreak Due to Infected Oysters. Fifty cases of typhoid in which it was reasonably certain that the infection was contracted from oysters are reported by P. B. Brooks,² of Norwich, N. Y., a district sanitary inspector. Cases appeared in certain municipalities as follows: Binghamton, 25; Johnson City, 10; Windsor, 6; Norwich, 5; Oxford, 3; and Greene, 1.

Of the various agents investigated, it was evident that water could not be a common source of infection, since each municipality had its own supply. Reports of bacteriologic examinations of the water supply of the city of Binghamton, made almost daily, did not indicate infection. In Binghamton the cases were scattered over the routes of nineteen different milk dealers. A clue which might have cast suspicion on the milk of one dealer came to naught when it was found that he was among the few who had no cases on their routes, and that he sold no milk except at retail. Naturally, at Thanksgiving time and at Christmas, a considerable number of persons had eaten celery. It was found, however, that there was no common source of supply, and investigation of a number of truck farms supplying celery led to its elimination.

The study to determine the possible relation of oysters to the outbreak proved most interesting and instructive. Incidentally, it was noted that there were no cases occurring among the very poor, of which class Binghamton naturally has its share. If water or milk had been the responsible agent, it might reasonably have been expected that the very poor, as well as those in comfortable circumstances, would have been affected.

It was found that thirty-eight patients, or 76 per cent. of the total number, fifty, were definitely known

(2) Jour. Amer. Med. Ass'n., May 6, 1916.

to have had oysters—a few having eaten them to excess—on a date consistent with the period of incubation. This period was determined by going back one week, and assuming that infection may have occurred at some time in the preceding two weeks. Most of the patients had eaten the oysters raw. In one instance they had been fried, and in others stewed.

It was found that the common practice, in preparing oyster “stew,” was first to “bring the water to a boil,” after which the oysters were added. They were not boiled, as this process is said to make them “tough.” It is apparent, therefore, that the process of cooking, as ordinarily practiced, is not likely to sterilize infected oysters effectively.

The results of investigation in the remaining twelve cases, or 24 per cent. of the total number, not included in the foregoing are summarized in the accompanying table:

CASES OF TYPHOID NOT DIRECTLY TRACED.

	No. of cases.
Oysters, raw, at about the date given as that of onset	4
Oysters, raw, at the right time but apparently not from the common source	1
Diagnosis apparently incorrect.....	1
Outside infection probable.....	1
Secondary	2
Not determined	3
Total	12

It is interesting to note, Brooks says, that, at the time of this investigation, oysters from a Maryland packer who supplied Binghamton dealers were under suspicion in connection with outbreaks of typhoid fever in three cities in Illinois.

Since a large number of persons other than those who developed typhoid ate oysters from the common source mentioned, while practically all of those who have been included as “oyster cases” had oysters from the same source, the inference is that, mixed with the oysters received by the two Binghamton wholesalers, were small quantities of infected oysters. From the incidence of the dates of onset, it may perhaps be as-

sumed that the infected oysters were included in two shipments, one about Nov. 1, 1915, the other shortly before Thanksgiving day.

To summarize: In November and December, 1915, fifty cases of typhoid fever occurred in six municipalities, in three of which there had been no cases in over ten months, and in one none in five months. There was apparently no possible common source of infection other than oysters purchased from various retailers, these retailers having been supplied by two of six wholesalers.

In twenty-seven of the definite oyster cases, the oysters were traced to one of these dealers; while those eaten by ten others came from the other dealer. In the thirty-eighth case the source of the oysters consumed was not determined. The two wholesalers received their supply from three Maryland packing houses, each of which drew for supply on a large number of small "shuckers" scattered throughout Maryland. Whether oysters from one "shucker" reached both the Binghanton wholesale houses remains to be determined if possible. Apparently the infected oysters were received in two shipments, one in November, the other in December. It may be added, in conclusion, that there have been no cases in these municipalities, other than secondary, since that time.

In a supplementary note to this article Brooks says that under date of April 5, 1916, he has been advised that it has been impossible to locate with certainty the source of the infected oysters responsible for this outbreak; that there are two small areas regarded as especially dangerous, one near the outfall of a sewer on which is a hospital, and that oysters from these areas were sold during the previous season.

TYPHUS FEVER.

Prophylactic Immunization. In a preliminary report of their work in the epidemics of typhus fever in Serbia, Bulgaria, Austria and Russia in 1915 and 1916, Harry Plotz, Peter K. Olitsky and George Baehr^s describe the

(3) Jour. Amer. Med. Ass'n., Nov. 25, 1916.

method by which a vaccine was prepared for prophylactic purposes, cite numerous instances in which this measure was used and show by their figures that there was an apparent definite benefit derived from it.

"The vaccine consisted of a suspension of fifteen strains of *B. typhi-exanthematici* in physiologic sodium chloride solution which had been subjected to a temperature of from 58° C. to 60° C. (136.4° to 140° F.) for from half an hour to one hour. After being tested aërobically and anaërobically as to its sterility, the vaccine was then diluted so that each cubic centimeter contained about two billion bacteria, and 0.5 per cent. phenol (carbolic acid) or tricresol added. Three injections consisting of 0.5, 1, and 1 c.c., respectively, were given in five or six day intervals.

"As the supply of vaccine was limited, it was considered advisable to restrict the vaccinations as far as possible to those persons who were most exposed to the danger of infection. The vaccine was therefore administered to the orderlies and members of the hospital staff who came in contact with the patients on or before admission to the hospital when they were still infested with lice, and also to the men whose duty it was to remove the clothing and bathe and shave the patients on admission, or who were concerned in the sanitation of villages or towns in which typhus fever was epidemic. In addition, many entire hospital units were vaccinated, and in a few instances small military groups in which typhus fever had broken out and was in danger of spreading."

In numerous institutions and groups of persons engaged in caring for patients with typhus, where from one to several cases of the disease had occurred among the doctors, nurses or orderlies, either no more or a very much reduced number of cases appeared following the prophylactic vaccination. Statistics were not obtainable where a considerable portion of the work was done, but the following summary is made from the figures that could be used:

In all, 8,420 persons, members of 109 hospital, sanitation and other units in Serbia, Bulgaria and Volhynia, were vaccinated against typhus fever during the epi-

demic of 1915-1916, an attempt being made to include in this number only the persons who were most exposed to the danger of infection. Of this number, six developed the disease during the four months of the epidemic. Experiences in the Balkans and Volhynia during the winter and spring of 1915-1916 with the vaccine made of *B. typhi-exanthematici* would seem, therefore, to indicate that it is capable of reducing the incidence of the disease, although it does not produce an absolute immunity to typhus fever.

Review of Literature. In a review of recent literature on typhus fever, Clyde B. Ker,⁴ lecturer on infectious diseases in Edinburgh University, refers to a considerable list of names, as those who have been most active in obtaining the knowledge of today in regard to this disease. He refers to the work of Plotz, who studied 300 cases of so-called Brill's disease, the endemic typhus fever of the United States, using aerobic methods with uniformly negative results. He then used anaerobic methods with cultivation, a procedure which does not seem to have been attempted by any previous investigator. Eleven cases of European epidemic typhus and forty cases of the local endemic fever were examined and it is said that in seven epidemic and eighteen of the endemic ones, the organism referred to as a positive agent was found in pure culture. Cultures made after the crisis in fifteen cases were negative, except in two instances. In one of these the bacillus was discovered twelve hours and the other thirty-six hours after the crisis. The organism found was a small, pleomorphic, Gram-positive bacillus, not mobile, not encapsulated, and not acid-fast. Its length varied from nearly 1 to 2 microns. No spores were produced. Polar bodies were occasionally observed, usually at one end of a bacillus. The organism was an obligatory anaerobe, and was killed by exposure to a temperature of 55° C. for ten minutes. This corresponded with the thermal death-point of the virus in typhus blood, as demonstrated by Anderson and Goldberger. Filtrates of an emulsion of cultures proved to be sterile, showing that the organism is not a filterable virus.

(4) Practitioner, September, 1916.

Olitzky, in making a study of the serum of cases of typhus fever, found that complement-fixing bodies were usually not seen at the height of the disease, but were demonstrable as the crisis was attained, and increased in concentration in the post-critical afebrile state. The same was true of precipitins and agglutinins. As regards the latter, agglutination was, in one case, obtained in a dilution as high as 1 in 1,000, thirty days after the crisis, and in 1 in 50 as late as 154 days after the crisis. Only three cases, out of thirty-eight studied after the crisis, gave negative results.

Plotz, Olitzky and Baehr found that of twenty-four guinea-pigs inoculated with the organism obtained from the blood of typhus patients eight, or 33.3 per cent., gave positive results, a bacillus, morphologically and culturally identical with that obtained from patients, being successfully isolated. Of four monkeys injected with the organism obtained from typhus fever, one developed the disease.

Hort, in discussing the bacteriology of the condition, considers that the most striking fact is the number of observers who have cultivated from the blood organisms of a diplococcal or diplobacillary nature. He does not consider the evidence produced sufficient to show that the organism is the cause of the fever.

Hort and Ingram are said to have demonstrated in and cultivated from fresh typhus blood, urine and cerebrospinal fluid a minute filter-passing organism which proved to be infective to monkeys.

This microorganism showed the same tendency to pleomorphism as the larger non-infective forms, which he considers the organism of Plotz to be. He also considers that the smaller organism does not persist as such in artificial cultures.

Hort states that definitely on two occasions clear filtrates of fresh fluids, containing both the smaller and the larger organisms, "showed on centrifuging small numbers of the minute organisms alone, whilst incubation of the same filtrates produced in a few days marked turbidity, due to the presence of large numbers of the *Bacillus exanthematicus*," which is the organism described by Plotz, Olitzky and Baehr.

The contention of Hort is that the larger organism found in the blood of typhus patients by Plotz and others is a less effective or non-infective form of a smaller and culturable organism.

Concerning the epidemiology of this disease it is stated that a number of investigators consider that the only means of transmission so far proven is by way of the body louse. Many other authors are quoted, however, as thinking that it may be transferred in the sputum by way of the urine, by contact with patients and in other ways that are not as yet thoroughly understood. It is considered by some authors that flies or other insects may be active in transmitting the disease in certain instances.

Isolation of the *Bacillus* of Typhus. A further study of the isolation of the *Bacillus typhi-exanthematici* from the body louse has been carried out by Peter K. Olitsky, Bernard S. Denzer and Carlos E. Husk.⁵

These men state that up to the time of their expedition for the study of typhus in Mexico, all cultural work on lice proved fruitless, and that correlations of most investigators in this field were based on purely morphologic data. One of the results of the Mexican expedition was the finding of the same organism in infected lice, growing it under anaërobic conditions and proving it to be the identical bacillus which Plotz reported as the etiologic agent in typhus fever, namely, *Bacillus typhi-exanthematici*.

The work here recorded, which was done in Mexico, had for its purpose the production of typhus fever in guinea-pigs by the intraperitoneal injection of infected lice, so that the nature of the reaction could be studied bacteriologically.

For this purpose, lice which were feeding on typhus patients were collected in a Stender jar containing a piece of sterilized cheese-cloth. They were ground up in a sterile mortar with about 4 c.c. of saline solution until a homogenous suspension resulted, and this was injected intraperitoneally into guinea-pigs.

Guinea-pigs that died following such treatment showed the typical lesions of typhus fever. These were orig-

(5) Jour. Amer. Med. Ass'n., April 21, 1917.

inally pointed out by Baehr and have been since thoroughly confirmed. They are as follows: No obvious lesion in any structure except the spleen, which is enlarged and congested, with its Malpighian bodies prominent. The spleens of these animals were emulsified in saline solution and cultivated anaërobically. After five days, twelve colonies of the typhus bacillus appeared in one of the culture tubes.

The conclusion to this phase of the work is that the transmission of typhus fever to guinea-pigs by the infection of typhus-infected lice has been accomplished and the typhus bacillus has been recovered from the spleen of a reacting animal.

Having proved that the lice which were regarded as being typhus-infected were capable of producing typhus fever in guinea-pigs and that from such guinea-pigs the typhus bacillus could be recovered, the culture of typhus lice was next undertaken. The medium used was 0.5 or 2 per cent. glucose agar to which one-third the volume of rich ascitic fluid was added. The medium and inoculated material were thoroughly mixed by being poured from one tube into another, after which the tubes were allowed to solidify in the upright position, and when solid were covered over with fluid agar.

Cultures from four series of lice were studied in New York, and were proved identical with endemic and epidemic strains of the typhus bacillus. Six series of lice from five different patients were cultivated. The number of lice in each series varied from two to six. The period of the disease when the lice were removed varied from the twelfth day of illness to the fourth day after the crisis. From practically all these lice, the *Bacillus typhi-exanthematici* was isolated, sometimes in pure culture, numbers varying from two to an innumerable number of colonies. In all the experiments made these lice were proved infectious. The organisms found in this work were found to be variable in their reaction to the Gram stain. The experience of the authors agreed with others in that the Gram-negative forms became Gram-positive on subculture.

In comparing this variability to the Gram stain with

that described in other organisms, they find that the literature offers several analogies.

In conclusion they state that since 1910 many observers in different parts of the world have reported the finding of an organism in typhus-infected lice. This organism they believe to have a causal relationship to typhus fever. Owing to the fact that improper methods have been used, the culture of this organism was impossible. In Mexico, the present workers have been able to grow this bacteria and to show that morphologically, culturally and serologically it is identical with the *Bacillus typhi-exanthematici*.

Research Work on Typhus. The infection of guinea-pigs with typhus and the results observed are recorded by N. T. Gamalieya,⁶ who calls attention to the fact that the blood of the infected guinea-pigs proved infectious during the very beginning of the disease. If this is the fact also in man, the persons infected would be dangerous from the point of view of infecting others, even when they were apparently still well. Another point to which he directs attention is the difference between the behavior of the typhus germ and other microbes (smallpox and rabies). The latter are not damaged by glycerine, and glycerine is often used to clear vaccines of foreign microbes. But the bacillus of typhus is extremely susceptible to the action of glycerine. Typhus organs subjected to the action of 80, 50 or even 30 per cent. glycerine lose their infectious power after twenty-four hours. Even with 20 per cent. glycerine, although the organs are not entirely sterilized, yet they are only weakly infectious thereafter. This sterilizing action of glycerine on the typhus microbe is so pronounced, this author says: "it justifies the administration of glycerine internally in treatment of typhus, especially as we know it is harmless."

Another peculiarity of the typhus germ is its susceptibility to low temperatures. Organs exposed to freezing temperatures lose their infecting power. This fact intimates, Gamalieya says, that winter temperatures will eradicate the infection in clothing, etc. Moreover, it indicates a special fragility of the typhus germ, as

(6) Russkiy Vrach, vol. 16, No. 12.

many other bacteria bear without injury very low temperatures. The facts here related seem to suggest, he adds, that if typhus is transmitted exclusively by the bite of the louse, it is because the microbe is too frail to be conveyed in any other way.

A Small Epidemic of Typhus Fever at Fort Madison, Iowa. This report is presented by Mark M. Boyd.⁷

The disease was brought in by a Mexican laborer who had come directly from El Paso, Texas. It was learned later that in this community in Texas there was a considerable amount of the disease about the time the Mexican laborer passed through that place. It was not until five days after he was admitted to the hospital that a macular eruption appeared over the trunk and extremities and a diagnosis of typhus fever was made. Previous to this time precautions against the disease had not been carried out to the strictness with which they might have been and one physician and three nurses became infected; one male nurse lost his life as a result of the infection. Altogether there were eight patients, seven of whom were shown to have been infected from the original Mexican laborer. The usual campaign against vermin was carried out, disinfection of all clothing and linen connected with the hospital at this time, and the epidemic was soon stopped.

As this epidemic was among the employees of the Santa Fe railroad and occurred in the hospital of this company, and as many of the laborers for the Santa Fe are Mexicans, and those who are not Mexicans are associated with this nationality, it was decided to carry out a campaign against lice throughout the system. A train was therefore equipped for this purpose. It consisted of four cars. The first was a freight car in which was constructed an oven heated by steam coils, in which clothing and bedding could be subjected to a dry heat in excess of 160° F. for the destruction of lice and nits. Storage space for supplies was provided in this car. Two heated bath cars in which Mexicans could be bathed in kerosene and soap suds were next in the train and a way car was also provided for the disinfecting crew of five Mexicans. This equipment was found so sat-

(7) Jour. Iowa State Med. Soc., February, 1917.

isfactory by the Santa Fe Railroad Company that the four cars have since been placed in operation, covering their lines in Illinois, Iowa, Missouri and Kansas.

Aside from this information on this campaign against the vermin which spread typhus fever, there is a good recapitulation of the literature on typhus fever in this article and some reference to its recent occurrence in Europe. Concerning the latter, the extent of the louse infestation on the western war front is given as follows:

4.9 per cent.	free from lice.
41.9 per cent.	harbored 1- 10 lice.
19.6 per cent.	harbored 10- 20 lice.
14.7 per cent.	harbored 20- 30 lice.
11.2 per cent.	harbored 30-130 lice.
4.9 per cent.	harbored 130-350 lice.
2.8 per cent.	harbored 350 and more lice.

In reference to the diagnosis of this disease, as encountered in this instance, three laboratory aids are of assistance according to this author. These are, (1) the negative Widal; (2) the leukocyte count, and (3) guinea-pig inoculation. A case presenting but a slight eruption may be difficult to distinguish from typhoid in the first two weeks of illness. This differentiation may be accomplished by the Widal test which is negative; by determining the existence of the leukocytosis; and by negative results with cultural examination of the blood and feces. A Widal test was performed on the blood from three of the Fort Madison cases with negative results in each case. Typhus cases present a leukocytosis ranging from 10,000 to 25,000. A leukocyte count on one of the cases in this article numbered 14,500. Guinea-pigs are susceptible to intraperitoneal inoculation with the blood of typhus patients. After an incubation period of from five to seven days, the pigs present a well-defined febrile reaction persisting for nearly two weeks. No changes are observable in the animal at post-mortem.

THREE-DAY FEVER.

Diagnosis of "Three-Day Fever." George C. Shattuck,⁷ of Boston, tells of observations made in the Paget

(7) New Orleans Med. and Surg. Jour., February, 1917.

Hospital in Serbia in the months of June and July, 1915. He said that at the beginning of the recent European epidemic of typhus, German physicians working in prison camps encountered a large number of cases of illness resembling influenza. By one it was observed from that ten to fourteen days before the development of typhus in many individuals there was headache, malaise, nasal catarrh, cough and sometimes angina, which disappeared in from three to five days. On account of the symptoms and the length of time between such attacks and true typhus, these cases were thought to be infections with some such organism as that of influenza. Seibert's opinion of the same condition is that mild cases of typhus without a rash may run a course suggesting influenza, and may be difficult to differentiate from it.

About the hospital at which the author worked there developed among the orderlies and others connected with it many cases of fever lasting three days more or less, and characterized by conjunctival injection, catarrh, reddening and slight swelling of the tonsils, frontal headaches, drowsiness, loss of appetite, malaise, with more or less pain and absence of eruption. Some cases otherwise similar showed a slight rash which faded out without becoming petechial, and this group was regarded as representing abortive typhus, so that it is altogether probable that some of these cases may have been abortive without a rash, if typhus can occur in this manner.

It was suggested by a physician from another part that these mild and apparently abortive cases might be instances of sand-fly fever. The duration of this fever varies from one to five, and perhaps to seven days; there is usually a leucopenia with a decrease of the polymorphonuclear cells, and the pulse-rate seldom exceeds 80, even with temperatures of 103° F. The onset is sudden with chilliness, nausea, headache, heaviness and discomfort about the eyes, lumbar pain and stiffness of the muscles of the legs, and somnolence. On the next day there is a fever of 101° and 102° F. The face is flushed, the conjunctiva injected, the tongue coated, and there is stiffness and pain in the back and calves of the legs, but no rash. The patient complains of frontal head-

aches and is mentally depressed. The leucopenia is slight.

The diagnosis of pappataci or sand-fly fever depends on the presence of the usual signs and symptoms, the existence of other cases, the occurrence in summer in a region where a sand-fly is found and the exclusion of other diseases by examination of blood films, negative germ reactions and sterile blood cultures. In view of the similarity of symptoms presented by the contagion confused as mild typhus fevers or influenza-like sickness, seen by the author during his work in Serbia, and of the fact that epidemics have been seen here by other investigators, it is his opinion that many of these patients suffered from sand-fly or three-day fever.

CHOLERA.

Solid Culture Medium for the Isolation of the Cholera Vibrio. The value of this medium, called a new culture medium for the isolation of cholera vibrio, by Graeme Ginson,⁸ depends upon the fact that this alone of all the intestinal organisms acidifies starch.

Owing to the medium possessing differentiating properties it should be especially useful in the detection of "cholera carriers," as the feces emulsified in broth can be plated directly on to it. In the case of water examination, after enrichment in peptone water for a few hours, if a drop or two of the peptone water is plated a tentative diagnosis can be arrived at in eighteen hours owing to the allied vibrios taking a longer time than the true cholera vibrio to bring about acid production.

Preparation of Medium. The formula is: Agar 30 grams, peptone 10 grams, starch 10 grams, sodium bicarbonate 1.5 grams, litmus (sufficient to color medium), and water 1,000 c.cm.

Weigh out 30 grams of powdered agar and emulsify with 250 c.cm. of cold water. Then weigh out 10 grams of peptone (Chapoteaut) and 1.5 grams of sodium bicarbonate. Mix together and emulsify in another 250 c.cm. of cold water. The two emulsions are then mixed in a two-liter flask and another 500 c.cm. of water added.

(8) Brit. Med. Jour., Sept. 30, 1916.

The solution is complete in the steamer. When dissolved the medium is clarified with white of egg and filtered in the steamer.

Weigh out 10 grams of potato starch, emulsify it with some of the filtered agar, and add the emulsion to the remainder of the medium.

The whole is sterilized by the fractional method, after which enough sterile watery solution of litmus is added to bring about a blue color of the medium.

The final reaction of the medium will be found to be —2 to phenolphthalein. Ginson tried several degrees of alkalinity and found that 0.15 per cent. sodium bicarbonate gave the best results.

If the plates are examined eighteen hours after inoculation, by looking obliquely through them with a dark background behind, the plate being held parallel to the window, the cholera colonies will be seen to have acquired a faint pink color, while the colonies of the other intestinal organisms are blue or of a whitish color. The examination is facilitated by the use of a hand lens. At this time the allied vibrios also produce blue colonies, but at the end of about thirty-six hours they also acidify the medium, though to a less extent than cholera.

At the end of from twenty-four to twenty-six hours the cholera colonies have attained a delicate pink color with a faint pink halo round them, while the other colonies still remain blue; also the colonies are of good workable size to pick off and proceed with the serologic tests.

After forty-eight hours, if the cholera colonies are in excess and the plate spread somewhat thickly, the medium itself becomes distinctly acid, and colonies other than those of cholera take on the pink tinge. However, the cholera colony even at this time can still be distinguished by the deeper red center which the other colonies lack.

The only other organisms which are known to acidify starch are some of the diphtheroid group and some of the non-pathogenic water vibrios. These should not present any great difficulty, as Gram's stain on the one hand, and the serologic test on the other, dispose of these organisms.

DYSENTERY.

Geographic Distribution of Amebiasis. The presence of amebiasis outside of the tropics and semi-tropics is thought by many to be rare. Medical literature contains, however, records of many instances, and even large numbers of patients that, so far as could be ascertained, had never been in the warm climates or in contact with individuals who suffered from amebiasis. An account of the patients seen with this disease at the Mayo clinic during the period from 1911 to 1916, with a record of the geographical distribution of the same, is given by A. H. Sanford.¹

In a review of the literature on this subject, with special reference to geographic distribution, it is shown that numerous instances have been recorded, not only in the temperate zones, but even in very cold climates; one from Alaska.

In speaking of the patients seen at the Mayo clinic he states that there have been 284 patients from Northern states in whom *Entamoeba coli*, the supposedly non-pathogenic organism, was reported. Five hundred thirty-five patients from the same district were found to be infected with *Entamoeba histolytica*. The majority of these patients were natives of the states in which they resided and all of them became infected while living in the northern portions of the temperate zone. As a control in this work, ninety-five patients from the South or the Orient in whom amebas occurred were studied. In the accompanying table are represented the geographical distribution of the patients, the number of patients, the kinds of organisms found, etc.

Further consideration of the work here presented brings out the following facts: Forty-one per cent. have constant diarrhea, and 33 per cent. have intermittent diarrhea, often alternating with periods of constipation; while nearly 26 per cent. have never had any bowel trouble except constipation. Occasionally these patients have ulcerations that are seen with the proctoscope, but the majority of examinations of this sort are negative. In fact, the entire syndrome is not so severe in the aver-

(1) Jour. Amer. Med. Ass'n., Dec. 23, 1916.

CASES OF AMEBIASIS

	Northern States and Canada																								Total Number of Patients, 1911-1916	Southern States and Tropics			
	Minnesota	Iowa	South Dakota	North Dakota	Wisconsin	Illinois	Michigan	Indiana	Ohio	Kansas	Nebraska	Wyoming	Colorado	Montana	Idaho	Utah	Oregon	Washington	New York	Pennsylvania	Massachusetts	New Hampshire	Maine	Saskatchewan			Manitoba	Alberta	Ontario
Constant diarrhea.....	51	41	30	25	16	8	6	1	2	1	9	1	1	8	1	0	1	2	1	1	0	0	1	8	5	3	1	224	20
Entamoeba histolytica.....	34	10	8	5	3	1	0	1	1	1	2	1	0	3	1	1	0	0	0	1	1	0	0	0	1	0	0	75	4
Entamoeba coli.....																													
Intermittent diarrhea.....																													
Entamoeba histolytica.....	38	42	23	8	11	7	4	4	1	3	3	1	1	12	0	1	0	3	0	0	0	0	0	6	3	2	2	175	20
Entamoeba coli.....	33	15	9	4		6	1	3	0	2	4	0	0	4	1	0	1	0	1	1	0	0	0	2	2	1	0	92	12
Constipation.....																													
Entamoeba histolytica.....	44	30	5	10	8	9	1	2	1	0	3	2	1	7	0	0	1	2	1	1	0	1	0	4	2	3	0	136	25
Entamoeba coli.....	29	27	15	12	4	8	4	0	1	2	0	0	0	3	0	0	0	1	0	0	0	0	0	2	3	1	0	117	14
Total Entamoeba histolytica	133	113	58	43	35	24	11	7	4	16	27	2	2	27	2	1	1	6	3	2	0	1	1	18	10	8	3	535	65
Total Entamoeba coli.....	96	82	32	21	13	11	5	4	2	5	9	3	1	10	2	1	1	0	2	2	1	0	0	4	6	2	0	284	80
Total amebas	229	165	90	64	48	35	16	11	6	9	25	5	3	37	4	2	2	6	5	4	1	1	1	22	15	10	3	819	94

age ameba-infected patient of the North as it is in those of the South or tropics.

The article includes some discussion of the possible sources of infection in the temperate zones, but no definite conclusions are arrived at as to how the organisms are spread. It is emphasized that it should be realized that this infection is general and that stool examinations are worth while with any patient with vague abdominal complaints or chronic diarrhea, no matter whence he comes.

[Numerous cases of *Entamoeba histolytica* have appeared in the Cook County Hospital at Chicago from the adjacent states.—GEN. ED.]

Pathology, Bacteriology and Diagnosis. In an article including these headings W. Magner² makes the following statements:

Both in amebic and bacillary dysentery secondary invasion of the ulcerated intestinal wall by organisms from the intestinal lumen is an important factor aggravating both the local and general condition. The pyrexia so frequently observed in the later stages of amebic dysentery is a result of this secondary invasion, and though usually toxic in origin may be due to bacterial invasion of the blood-stream. A similar septicemia may occur in the bacillary type of the disease.

Amebic dysentery may be latent, the ulcers being confined to the cecum and producing no symptoms. Apart from the danger of the disease becoming active such cases may act as foci for the spread of the disease.

Every case of amebic dysentery should be treated by the administration of at least 10 grains of emetine. Incomplete treatment may result in the patient becoming a cyst carrier and a danger to the community.

The prevention of amebic dysentery depends upon the elimination of cyst carriers, rapid and complete disposal of fecal matter, and protection of food from dust and flies.

In bacillary dysentery the earliest pathologic change in the intestinal wall is dilatation of the vessels and a marked hemorrhagic exudation into the submucous coat.

(2) Lancet, Oct. 21, 1916.

Leukocytic accumulation is a later phenomenon resulting on necrosis of tissues.

Mannite-fermenting dysentery bacilli can exist in the intestine in an avirulent form. The presence of such an organisms in the stools loses much of its significance in the absence of a positive Widal reaction.

The agglutination reaction in dysentery is a valuable means of differentiating the bacillary type of the disease. In the Shiga infections specific agglutinins are invariably present after the first week of the disease. Distinct agglutination with a serum dilution of 1 in 100 is diagnostic.

Judging from serologic tests it would appear that certain organisms, normally saprophytic, may in both types of dysentery stimulate the production of specific agglutinins as the result of invasion of the ulcerated intestinal wall.

The toxins of Shiga's bacillus are highly pathogenic to rabbits. Subcutaneous injection with either living or killed cultures results in the development of paralytic symptoms and death. The characteristic lesions of the human disease can not be readily reproduced.

Result of Research. An epidemiologic and bacteriologic investigation of dysentery and para-dysentery infections in California has been carried out by K. E. Meyer and J. E. Stickel of the George William Hooper Foundation for medical research. They give a brief review of the literature concerning similar work elsewhere in this country and also extensive detail as to the work carried out at various points in California. This includes the report of numerous family epidemics.

The conclusions reached in this work are:

Para-dysentery, caused by para-dysentery bacilli of the Hiss-Y-Russel type (Group I), the Flexner type (Group II), and the new, well-defined type (Group III. Sonne), exists in epidemic or endemic form in California.

Infantile diarrhea is in some cases due to para-dysentery bacilli and should be frankly designated as "infantile dysentery."

Bacteriologic stool and blood examinations, according to a definite working scheme, should be supplemented by agglutination tests of the patient's serum.

In making an investigation and a true diagnosis of patients suffering with dysentery it is emphasized that systematic stool examination in acute and chronic cases of colitis is very important.

Dysentery and Diarrhea in Egypt. A special form of diarrhea with peculiar gastric symptoms which occurred among soldiers in Egypt, is described by G. Marshall Findlay.⁴ He says that of the Europeans who arrive in Egypt for the first time, it is probable that nearly 90 per cent. suffer from a form of diarrhea associated with gastric symptoms, which is so common that it is known among Anglo-Egyptians as "Egyptian stomach-ach." The first attack usually comes on within a fortnight after arrival in the country, while subsequent attacks may recur at intervals of from one to two weeks. After a residence of roughly six months the disease entirely subsides and does not again appear. Owing to the comparatively slight symptoms the condition has failed to attract any great notice among specialists in tropical medicine.

A typical attack of this condition usually begins in the early hours of the morning, although it may commence at any hour of the day or night. At first there is only slight abdominal uneasiness, but this is quickly followed by definite griping pains, confined for the most part to the epigastric and umbilical regions. There is a marked desire to empty the bowels, though evacuation gives little relief. As many as ten or fifteen stools may be passed during the day. Nausea and vomiting are present in about three-quarters of the cases, and in a few instances headache is a marked symptom. The temperature is slightly raised in the evening—from 98.8° to 99.8° F., while the posterior part of the tongue is covered with a brownish fur. Diarrhea does not persist for more than two or three days at the outside; it is usually followed by constipation. About a week generally elapses before the bowels begin to regain their normal action. A similar attack may recur within a fortnight or three weeks of the original attack. The feces are always fluid in character and in a typical case resemble pea soup. Blood and mucus are absent. The blood shows no defi-

(4) Lancet, May 19, 1917.

nite changes except a slight but constant increase in the large mononuclear leukocytes (10-18 per cent.).

The condition was not found confined to any particular class. Aside from this gastric disturbance, the second and most important cause of sickness among naval ratings has been amebic dysentery. Cases of this condition are said to be separated into, old dysenterics who have relapsed, and first attacks in persons who have never been abroad. In the group of patients considered here the former class constitute nearly 20 per cent. of the total number; and as in the majority of instances the dysentery was first contracted in Gallipoli, during the Dardanelles campaign, these individuals must have been acting as convalescent carriers since that time. Apart from the condition of the stools, the clinical symptoms seen here were very similar to those described as occurring in the condition known as "Egyptian stomach."

The first attacks of dysenteric symptoms do not, as a rule, manifest themselves until the patient has been a resident in the country for a few weeks at least.

An inquiry into forty cases of dysentery occurring for the first time elicited that in thirty-six of these there was a previous history of one or more attacks of "Egyptian stomach," preceding the onset of dysenteric symptoms. The intervals elapsing between the last attack of "Egyptian stomach" and the commencement of the dysentery varied from a few days to some months.

In order to determine whether there was any relationship between the two conditions a microscopic examination of the feces was carried out in 110 cases of "Egyptian stomach." In regard to the presence of entamebas, the following results were obtained:

<i>Entamoeba</i> entirely absent.....	8 cases
<i>Entamoeba coli</i> present	10 cases
<i>Entamoeba histolytica</i>	36 cases
<i>Entamoeba minuta</i> (Elmassian)	49 cases
<i>Entamoeba minuta</i> (Elmassian), together with tetragena cysts	7 cases

Method of Concentrating, Culturing and Counting *Entamoeba* Cysts in Stools. Working under the direction of Lieutenant-Colonel Sir Ronald Ross, J. W. Crop-

per and R. W. Harold Row⁵ have perfected methods of concentrating the cysts of *Entamoeba* in stools for diagnostic purposes (Fig. 6).

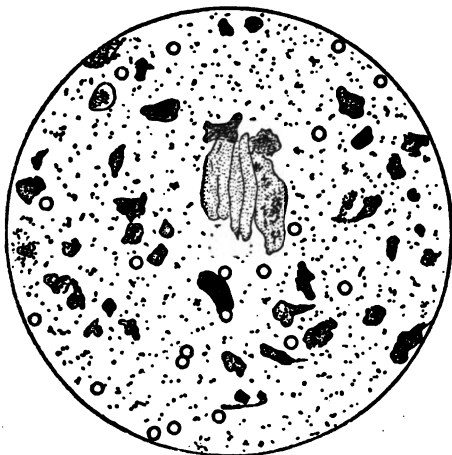


Fig. 6. Maximum concentration of *E. coli* cysts in stools by the ether method. One field. Lower power: $\times 50$.

For the maximum concentration of the cysts the following method is given:

"A lump of feces, which should be at least 1 gram in weight, is shaken up with about 30 c.c. of normal saline (0.8 per cent. solution of NaCl) per gram of feces for a sufficient time to disintegrate the mass into individual particles, and thereby form an emulsion which will settle only very slowly. This is best done on a mechanical shaker in a large flask or bottle of a capacity of at least four times the amount of fluid to be shaken, and we have found it necessary, in order to obtain the best results, to continue the shaking for a minimum of half an hour.

"The emulsion is then poured into a separating funnel and shaken up, by hand, for a half a minute with from 10 to 20 per cent. of its volume of ether (ordinary methylated ether is perfectly suitable for this), after which the mixture is allowed to stand for a minute or

(5) Lancet, Feb. 5, 1917.

two in the funnel until the two liquids have separated. The fecal *débris* absorbs ether and consequently becomes lighter than water, and, when separation is complete, lies in a mass at the top of the saline, immediately below the excess of ether. The cysts are not affected by the ether, and consequently remain in the saline beneath.

"The saline fluid is then drawn off from the separating funnel, and is centrifuged at a slow speed for two or three minutes, the precise time required necessarily depending upon the rate of centrifugalization and the size of the tubes. By this means the cysts will be brought down to the bottom of the tubes with the comparatively slight amount of fecal matter not taken up by the ether.

"For ordinary diagnostic purposes the concentration now effected, which should be some fifteen times as rich in cysts as the original material, will be found adequate, but, if desired, a still greater proportion of cysts can be obtained by decanting the supernatant liquid and filling up the centrifuge tubes with normal saline, shaking thoroughly, and submitting the tubes to fractional centrifugalization, the material brought down in the first 10 seconds being discarded, and the whole time of centrifuging curtailed by half. By repeating this process two or three times the maximum concentration is obtained, and the *débris* still remaining consists almost entirely of particles of practically the same size as the cysts themselves."

For the relative concentration of cysts for cultivation a different technique is given:

"Ten grams of feces are shaken with 100 c.c. of normal saline in a bottle or flask on a mechanical shaker for five minutes to obtain a uniform emulsion. This is poured on to a layer of fine silk whose mesh is of the size mentioned above, and which is stretched on a tambour (such as is used by milliners), and the emulsion is gently and continuously stirred with a glass rod to prevent the clogging of the meshes of the silk. The residue left on the filter consists chiefly of large lumps and stringy matter, and is discarded. It contains only a small percentage of cysts, which can be still further reduced, if required, by washing. The filtrate (or a portion of it) is then centrifuged for one minute at a speed of

1,200 revolutions a minute, the supernatant liquid poured off, and the volume made up again with normal saline. The tube is then well shaken, and again centrifuged as before. This process is repeated until the supernatant liquid is almost clear. Finally the deposit is shaken with 10 c.c. of normal saline and is allowed to stand

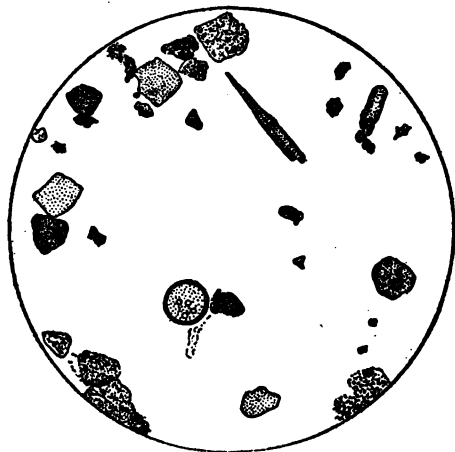


Fig. 7. All visible particles and a 4-nucleate cyst of *E. coli* in one field of an emulsion prepared by the method of relative concentration for cultivation experiments. High power: $\times 275$.

for a few minutes. The upper portion is then poured off and is thoroughly centrifuged, and loopfuls of the deposit are used to make hanging-drop preparations for culture experiments." An illustration (Fig. 7) is given of a high-power view of the appearance of cysts and débris in such a preparation.

"By this means cysts are obtained which have been thoroughly washed free from toxic bacterial products, acid substances, and other deleterious matter present in the original feces. The cysts can be found easily with low powers of the microscope, and are not subsequently lost, even though it is necessary to keep the preparations for several days in the incubator. *Amoeba limax* cysts submitted to this process have been subsequently cultivated without difficulty, and were evidently unaffected either by the shaking or the centrifugalization."

To count the cysts in stools the following outline of technique is given:

"A uniform emulsion of 10 grams of stool (selected from several different portions of the bulk) is made in 100 c.c. of normal saline (*i. e.*, 10 per cent. weight ÷ volume) by shaking on a mechanical shaker for 10 minutes. All soft masses are broken up in this way, and the sediment which falls consists only of gritty particles, the so-called "false sand," which microscopic examination shows to contain no cysts.

"A capillary pipette is made and is calibrated to deliver 20 c.mm. in a length of about 2 inches. It is provided with a rubber teat. It is well to have several of these pipettes ready to hand, so that successive counts can be made with a dry one without any unnecessary delay. The pipette supplied with Gowers' hemacytometer, and other similar ones which are on the market, can be used for the purpose, but they have a somewhat narrow bore and frequently become clogged with débris. There is little risk of any cysts being retained in a pipette made according to the above instructions when the mixture is blown out: in fact, we have not yet found a single cyst in the washings out after use.

"Several glass slides, 3 inches by 1½ inches, having been prepared with a ring of vaseline 1 inch in diameter, a measured volume (20 c.mm.) of the emulsion of feces is drawn into the pipette and is placed in the center of the ring.

"A cover-slip ruled in squares, such as is used with Böttcher's slides, is then allowed to fall gently, with the engraved face lowermost, flat on to the drop of emulsion, and, if necessary, is pressed down to diminish the depth of the layer of liquid. The count is made with a low power. The cysts which happen to be in any portion of the drop which extends beyond the squares are easily counted, and are indicated in the count by the letters A, B, C, etc. The squares themselves are numbered as shown (the reverse way up) in the diagram (Fig. 8)."

The author states that he has made sufficient experiments to establish the utility of the method for counting entameba cysts in feces, and sees no reason why its

employment should not be extended, with such modifications as are found necessary, to the counting of other protozoa, either in their natural surroundings or under different conditions of cultural environment.

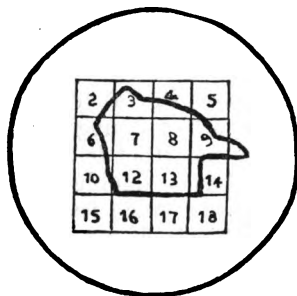


Fig. 3. Diagram to show the method of counting entameba cysts in stools. The edges of the large drop of 20 c.mm. of faecal emulsion are indicated by the thick irregular line, and all cysts in this drop are counted with a low power. $\times 1 \frac{1}{3}$.

Amebic Cysts. Their Importance from a Diagnostic and Pathologic Viewpoint in Amebic Dysentery. P. Ravaut and G. Krolunitski⁶ say that if one relies solely on finding amebas to establish a diagnosis of amebic dysentery, the disease will commonly not be recognized, as the period during which they are eliminated is relatively very brief. On the other hand, cysts may be sought during the entire course of the disease and in material several days old.

Feces may be examined fresh or preserved with formalin. For this purpose, a portion is diluted with physiologic salt solution and spread between slides; the specimen may be fixed by osmic acid vapor and stained with hematoxylin or examined without staining. Cysts are recognized by the following characteristics: A double cyst wall, a high degree of refraction, the character of the nuclei, the borders of which are outlined by fine granulations.

Of the amebas, *E. coli* is non-pathogenic; *E. histolytica* and *E. tetragena* are pathogenic.

The cysts of *E. coli* are always at least 16 μ in diam-

(6) Presse méd., July 3, 1916.

eter, commonly 16-25 μ , the nuclei number from one to eight.

The cysts of *E. histolytica* and *E. tetragena* never measure more than 14.5 μ in diameter, commonly 10-14.5 μ , the nuclei are from one to four—never more than this. The cysts of *E. histolytica* are often oval, and to get the diameter one measures both dimensions and takes the mean.

If no cysts are found after at least six searches, they may come down after a brisk purge.

Other parasites that may lead to confusion are: *Blastocystis hominis*; this has a double wall, but the space between the walls is very much less than in the amebic cysts. *Lambia intestinalis* has a double wall, but the nuclei have no granular border and, moreover flagella may be seen coiled within.

Beside being a most important means of diagnosis, the examination of feces for cysts is a most important check on the reaction to treatment. For example, the authors claim to have found that arsenic is of more value than emetine; and that a combination of the two causes the most rapid disappearance of the cysts. Furthermore, the recognition of cysts is extremely important in detecting carriers of amebic dysentery, since many of the territorial troops come from regions of endemic amebic dysentery and epidemics are already breaking out among the French troops.

Stool Examinations in Dysentery and Diarrhea. The results of this work on the stools of 422 patients is published by Lieutenant-Colonel C. J. Martin and Sister F. E. Williams.⁷

No. 3 Australian General Hospital being a base hospital, in a large proportion of the 422 cases examined the acute stage of the illness was over and the patients were passing normal or merely loose motions, but in 217 cases the stools contained muco-pus in some amount, with or without blood, at the time of the examination. All specimens were examined for protozoologic parasites, but only when mucus was present was the isolation of dysentery bacilli attempted.

(7) Brit. Med. Jour., April 14, 1917.

PLATE I.



Portion of colon showing an isolated group of amebic ulcers. The drawing shows that the mucous membrane of the colon, apart from the group of amebic lesions, is intact. The group of ulcers is prominent; it appears to stand up from the level of the mucous membrane. The ulcers contain the typical yellow necrotic debris which indicates that amebas are present. There is a small slit-shaped ulcer on the summit of one of the rugae.—Martin and Williams (see page 98).

PLATE III.



Portion of colon showing "pure bacillary" dysenteric lesions. The drawing shows extreme congestion of the mucous membrane with patches of green diphtheroid membrane on the surface. There is a shallow serpiginous ulceration involving the superficial part of the mucous membrane; but there is none of that deep undermining of the mucous membrane which has been illustrated in amebic lesions. There might, however, be deep ulceration obscured by the patches of diphtheroid membrane. Such deep ulcers containing amebas were found in some intestines of this type. In this case amebic ulcers were not found, and it is classed as a "pure bacillary dysentery."—Martin and Williams (see page 98).

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TABLE OF RESULTS.

Total cases 422.

<i>Amoeba histolytica</i> or its cysts.....	72
<i>Amoeba coli</i>	29
<i>Lambia intestinalis</i>	33
<i>Tetramitus mesnili</i>	14
<i>Trichomonas intestinalis</i>	16
Coccidia (Isospora)	1
217 Cases passing mucus with or without blood:	
<i>Amoeba histolytica</i> or its cysts.....	63
<i>Bacillus dysenteriae</i> , Flexner group.....	64
Bacilli indistinguishable culturally from Flexner group	12
<i>Bacillus dysenteriae</i> , Shiga.....	47

No grounds were discovered for supposing that any of the protozoologic parasites present, except *Amoeba histolytica*, were responsible for ill health. Twelve organisms isolated resembled the Flexner group of bacilli culturally and biochemically, but failed to agglutinate with any Y or Flexner serum obtainable; eight of the strains were retested against the same serum six months later, when five of them agglutinated quite well.

Pathology of Dysentery in the Mediterranean Expeditionary Force. A most elaborate article on this subject is presented by G. B. Bartlett,⁸ of the Pathological Institute of the London Hospital.

The material on which this investigation is based was obtained during the last half of 1915 and the first two months of 1916, when the author was pathologist to No. 21 General Hospital. This unit arrived at the end of May, 1915, and began taking in cases about the middle of June. The patients were nearly all from the Gallipoli peninsula or from Mudros. At first the cases were mainly surgical, but as the campaign in Gallipoli progressed the medical cases increased in number until, at the end of the year, the cases were almost entirely medical.

The chief epidemic diseases were enteric fever and dysentery. During the last six months of 1915 the admissions on the medical side were 5,300 in number. One thousand seven hundred and twenty-three were classed as enteric; of these 98 died, giving a mortality of

(8) Quart. Jour. Med., April, 1917.

5.688 per cent. One thousand one hundred and forty-six cases were classed as dysentery. (This number does not include patients admitted for wounds, etc., who were suffering from mild dysentery or who developed clinical dysentery subsequent to their admission. Nearly everybody on the peninsula suffered from diarrhea, and cases were not classed as dysentery unless there was tenesmus, and blood and mucus were passed, or unless pathogenic amebas or dysentery bacilli were found in the feces.) Fifty-six patients died from dysentery, giving a mortality of 4.886 per cent. (This number does not include patients who died from wounds, etc., and were found in the post-mortem room to have dysenteric ulcers.) Thus more than half the medical cases during this period were classified as enteric or dysentery.

The epidemic of dysentery was severe from August to December, 1915. The epidemic was present before August and after December, but it was during these months that the epidemic was severe. The "bloody flux" then sent a great number of men from the peninsula.

The author presents the following general summary of his work:

The epidemic of dysentery among the troops upon the Gallipoli peninsula was due to amebic infection.

In the examination of 477 stools which had the appearance of dysenteric stools, vegetative amebas of pathogenic type were found in 379, or 79.4 per cent. At the post-mortem examination of 61 cases of dysenteric ulceration of the intestine, amebic lesions were found in 56, or 91.8 per cent.

Amebic infection was more prevalent on the peninsula than the symptoms and signs in the hospital indicated. In the routine examination of 652 stools which had not the appearance of dysenteric stools, vegetative amebas of pathogenic type were found in 118, or 18 per cent. In 11 of the 56 cases in which the amebic lesions were found at post-mortem examination there had been no signs or symptoms of dysentery while the patients were in hospital. Comparisons of the lesions with the length of stay in hospital showed that infection contracted in hospital was excluded in almost all these cases.

An indication of the prevalence of amebic infection

in the troops is given by the results of the total number of routine examinations of feces and post-mortem examinations. Between June, 1915, and February, 1916, 1,129 specimens of feces were examined; vegetative entamebas of pathogenic type were found in 497, or 44 per cent. During the same period, 142 complete post-mortem examinations of the body were made; the head was not always examined. Amebic lesions were found in fifty-six, or 39.4 per cent.

The epidemic of amebic dysentery was accompanied by an epidemic of enterica.

Lesions of enterica were found in forty-one of the 142 complete post-mortems, or 28.8 per cent.

Amebic dysentery associated with enterica infection was relatively common. In the fifty-six cases in which amebic lesions were found on post-mortem examination enterica infection occurred in 9, or 16 per cent.

In the nine cases in which both amebic dysentery and enterica infection were present, acute or healed enteric lesions, together with amebic ulcers, were found in the intestines in seven; amebic ulcers alone were found in two. In the latter two cases infection by paratyphoid *B* was demonstrated by agglutination before death and also in one case by culture after death. The condition of the glands and spleen was such as is found in enterica infection.

Amebic lesions in the intestine were very frequently associated with a secondary bacterial infection of varying intensity. This secondary infection led, in some cases, to a septicemia of intestinal origin.

In some cases this secondary infection was very intense, so that the amebic lesions were obscured by a diphtheroid inflammation resembling that found in bacillary dysentery.

In five cases an inflammation of this kind was present alone, no amebic lesions being detected.

Inasmuch as amebic ulceration may be complicated not only by enteric but by secondary bacterial infections it is essential that, for the complete elucidation of any case of dysentery, all possible methods of investigation should be employed. The examination of feces and post-

mortem material for amebas must be supplemented by bacteriologic and serologic investigation.

On the other hand, the employment of bacteriologic and serologic methods alone will give an entirely erroneous idea of the initial infection in amebic dysentery. Examination of feces for amebas and post-mortem examination can not be dispensed with in the investigation of dysentery.

The bacteriologic and serologic investigations in the series of cases examined post-mortem were, unfortunately, very incomplete. They give no indication of the number of cases in which secondary inflammation in intestines showing amebic lesions was caused by bacilli of the dysenteric group. When the complicating infection was intense and resembled that seen in bacillary dysentery it has been tentatively diagnosed as "bacillary dysentery." In only one of the five cases in which amebic lesions were absent and an inflammation of this type was present was there evidence of a specific infection by organisms of the dysentery group. These five cases have been tentatively called "pure bacillary dysentery."

Allowing the tentative diagnosis mentioned in the preceding paragraph, the sixty-one cases of dysenteric ulceration examined in the post-mortem room may be classified according to infections as follows:

- (a) Pure amebic ulceration—41 cases, or 67 per cent.
- (b) Amebic ulceration and enterica infection—7 cases, or 11.4 per cent.
- (c) Amebic ulceration plus enterica infection plus dysenterica infection—2 cases, or 3 per cent.
- (d) Amebic ulceration plus dysenterica infection—6 cases, or 9.8 per cent.
- (e) Pure dysenterica infection—5 cases, or 8 per cent.

The routine treatment (injection of emetine hydrochloride, administration of saline purgatives and bismuth mixture, with rest in bed and careful diet), recommended by Sir Ronald Ross, was successful in curing amebiasis in the majority of the cases; in some cases a thorough administration of the treatment failed to eliminate amebiasis.

In some cases treated in this way, although vegetative

amebas disappeared from the stools, purulent diarrhea persisted.

This persistent diarrhea was due to the persistence of secondary bacterial inflammation. Thus a special group of cases was found post-mortem in which the treatment applied in the wards had been on the average most thorough and in which after death no amebas were found in the tissues. Many of the amebic lesions were healing or healed, but secondary bacterial inflammation was specially pronounced.

It is most important, therefore, that specific treatment should be administered early so that the amebic ulceration may be arrested before it has rendered the colon more vulnerable to secondary bacterial invasion.

It is further important that the routine treatment in amebic dysentery should be designed not only to eliminate amebiasis but to combat bacterial infection of the intestines. The saline purgatives and bismuth mixture in the treatment adopted proved of service in this respect. If an antiserum is employed it should be polyvalent.

In addition to secondary bacterial inflammation of the intestines the most serious complications of amebic dysentery were: Intestinal hemorrhage, intestinal perforation, septicemia of intestinal origin, amebic abscess of liver (5.3 per cent.), and broncho-pneumonia. Of these, hemorrhage was the most frequent.

Amebic ulceration may be present in patients who present no signs or symptoms of dysentery.

In the examination of stools for protozoa, and in particular for vegetative entamebas, microscopic examination of unstained material should be supplemented by examination of films fixed when wet and subsequently stained.

In the feces and in the tissues vegetative entamebas are frequently associated with "refractile cells."

The "refractile cells" represent a stage in the life cycle of the pathogenic entameba. Their presence is, therefore, of diagnostic value.

The appearance of the colon when infected by pathogenic entamebas varies greatly both in different areas in individual cases and in different cases.

This variation depends on the intensity of the amebic infection, the stage of the infection, and the degree to which the amebic lesions are complicated by bacterial infection. In certain cases the amebic lesions are obscured by such secondary inflammation and can only be revealed by section of the gut.

In lesions of certain type, particularly the smaller lesions, amebas are much more likely to be found.

In order, therefore, to ensure the detection of amebic infection in the post-mortem room the colon must be examined with great care, small ulcers and foci of diphtheroid inflammation should be incised, and a number of the smaller lesions should be selected for microscopic examination (Plates I, II and III).

In order to determine the presence of vegetative entamebas and refractile cells in post-mortem material, microscopic examination of scrapings from ulcers and of blood-films from the dilated subserous veins is a valuable supplement to the examination of sections of embedded material; it enables a large number of lesions to be examined rapidly.

Such scrapings and blood-films should be examined, as in the case of feces, both in unstained films and in films fixed when wet and subsequently stained.

Rapid Method of Detecting Protozoal Cysts in Feces.
In order to reduce the amount of time spent in the examination of film preparations of feces for protozoal cysts Robert Donaldson⁹ has devised the following stain mixtures which he states render it almost impossible for even a novice to fail to detect the presence of the cysts.

After trying various proportions, it has been found that a mixture of equal parts of the two stains used in any of the three following combinations will yield the best results.

A. Five per cent. aqueous solution of potassium iodide saturated with iodine to which is added an equal volume of either—

- B. (1) A saturated aqueous solution of rubin S; or
(2) a saturated aqueous solution of eosin; or
(3) Stephens's scarlet writing fluid.

(9) Lancet, April 24, 1917.

(*Note*.—1. It was found necessary to specify this particular brand of red ink, as some brands are useless for the purpose. 2. Basic fuchsin can not be used.)

A few loopfuls of one of the above stain combinations are placed on a clean slide, a loopful of feces taken and rubbed up with the stain to form a fairly smooth suspension, and a clean cover-slip gently lowered over the drop. To get the best possible definition it can not be emphasized too strongly that the film so made should spread out under the cover-slip by capillarity so as to form the thinnest possible layer—preferably a layer which is no thicker than the diameter of a *coli* cyst. Obviously, no gross particles must be left in the film, otherwise the cover-slip will not lie flat. The exact amount of stain to place on the slide will soon be learned after one or two attempts, and will depend on the size of the platinum loop employed and the size of the cover-slip. It is also preferable, although not essential, to mix afresh for each day's use the two elements of the combination stain.

The stain combinations here recommended are devised for the purpose of detecting protozoal cysts in general and more particularly those of *E. coli* and *E. histolytica*, but they are not intended as a means of discriminating between *E. coli* and *E. histolytica* cysts respectively, although there are some indications that this mode of staining may aid in the differentiation. To get the best results attention must be paid to the various points mentioned. The advantages claimed for the above technique are these:

One or other of the stain combinations can easily be obtained and rapidly made up.

The detection of cysts and their identification are carried out in one and the same preparation.

The contrast in color is so striking that the cysts cannot be mistaken for anything else and the veriest tyro can not fail to detect them if present. The possibility of missing a carrier is reduced to a minimum.

Without using too thick a preparation, it is nevertheless possible to use slightly more feces at one examination than by the simple iodine method. The cysts can be picked out quite easily even in a thick clump of

débris, and this is not always possible in a simple iodine preparation.

Where doubt exists as to whether a particular cyst is to be classified as *E. coli* or *E. histolytica*, accurate measurement—formerly considered a point of crucial importance but no longer to be relied on—is facilitated, since the effect of halation is practically eliminated.

The method above described reduces considerably the time spent on such examinations, a point of some importance where many specimens have to be examined in a day. A positive film even in the hands of the less experienced can be recognized at once, while a negative film may be labeled so with certainty inside two minutes.

Where the observer is hunting specially for the smaller cysts, such as those of *Tetramitus mesnili*, the Stephens's ink combination may be found preferable, although it does not give such a definite color contrast with the larger cysts. In all cases the film made should be the thinnest possible, and the source of illumination should be taken into account.

Treatment of Carriers of Amebic Dysentery with Emetine Bismuth Iodide. The authors of this article, W. Waddell, C. Banks, H. Watson, and W. O. Redman King,¹⁰ discovered the patients whose cases are here discussed to be carriers of *Entamoeba histolytica* in the course of the ordinary routine examination of feces at a convalescent hospital. None was found to be a carrier of dysentery bacilli. They were all treated with emetine bismuth iodide, and the authors think it worth while to publish a report as it is the first time to their knowledge that the drug has been tested on such a large scale. The treatment has had the advantage of being carried out under the supervision of one medical officer at a place where the necessary protozoologic examinations could be made on the spot.

All the patients came into the hospital as convalescents after dysentery; fifty-two came direct from hospital ships, the others from home hospitals.

With nine exceptions the men were all invalided from the Eastern Mediterranean area (87 cases) or Mesopotamia (6 cases). The other nine were invalided

(10) Lancet, July 21, 1917.

from France; of these five had had dysenteric symptoms in Egypt and two in Gallipoli, while another had contracted dysentery in India in the autumn of 1914 just before being sent to France with a division of Indian troops. Of the other patient from France the authors have no further details. Two men had previously had dysentery in India in 1908 and 1914 respectively, but as one had subsequently been sent to Saloniki and the other to Gallipoli, it is impossible to assert with certainty that either had become infected with *Entamoeba histolytica* in India. Two men had had dysenteric symptoms in Africa, one in 1881 and the other during the Boer war; a third had had either "dysentery" or "enteric" during the Boer war. Three men reported having had diarrhea with blood and mucus in France for a few days before going to Saloniki or Gallipoli, but it is impossible to say whether it was of amebic origin. Seven men who had dysentery in Gallipoli afterward were sent to Saloniki, where they relapsed.

One man had no history of acute dysentery, but he was invalided from Saloniki to Malta with nephritis and while in hospital there was found to be passing cysts of *E. histolytica*; there seems to be no doubt that he was a contact carrier.

A large number of these men had been treated with emetine hypodermatically, one or two having received as many as 100 injections. One man had been operated on for liver abscess.

In treating these cases the authors used a keratin coated tablet containing grain of emetine bismuth iodide.

As a rule, the daily dose, consisting of three grains, was given to each man after the mid-day meal. This time was decided on by the men after trials of various hours. They found that they were less disturbed by taking the dose at mid-day than at any other time and objected strongly to its being given at night owing to night calls to the latrine.

After taking the drug they lay down and rested; during the earlier part of the day they were allowed

out within the lines, and being dressed in blue they were easily kept under observation.

Each man was provided with a card on which were noted the daily dose and the results, number of times vomiting occurred and number of bowel evacuations. Each daily dose was administered by the medical officer's own hands. All the men were placed under the same living conditions. The diet adopted consisted of milk, eggs, fish, puddings, mutton, and cabbage, strained and sieved.

The effect of the drug was very much the same in all cases. There was purging, vomiting or both. Usually a man who vomited did not have much diarrhea and *vice versa*; and usually whichever symptom predominated at first remained the chief symptom throughout. Very rarely was any man violently attacked both ways. Two men had violent colic and required hot fomentations.

Various stomach and bowel sedatives were tried to control the irritation; but none was of any real use except tincture of opium, and that was only used in extreme cases. It was noted that in the vomited material the brick-red color of the drug was seen, showing that the keratin coat dissolved before reaching the intestine.

The tabloids were tried in powder, but vomiting was produced sooner and increased in intensity, so this method of administration was discontinued. In three cases of old carriers, the effect on the general health was most pleasing. All three were weak, pale, and depressed, but after the treatment the appetite returned, weight was regained, and all three reported that they felt like new men. In most cases, however, the men were for the time considerably pulled down by the vomiting and diarrhea. All were heartily glad when the ordeal was over and they were set free.

The article contains tables showing the amount of the drug received by each man, the period of treatment, the number of doses, the amount of vomiting and diarrhea produced, and a list of the tests made before and after treatment. These tables, the authors state, show the curative properties emetine bismuth iodide

certainly possesses; but till its preparation has been improved, and its intensely irritating properties abated or removed, a just estimation of its value in chronic dysentery can not be made.

They present the following conclusions:

Emetine bismuth iodide is much more effective than emetine hydrochloride in the treatment of carriers of *Entamoeba histolytica*, but about 20 to 25 per cent. of failures may occur.

The intensely irritating properties of the drug in many cases are a drawback to its general application.

The definite failure to cure nineteen out of the one hundred and two cases treated at Barton may perhaps be in part due to the form of the drug employed (a keratin-coated tabloid).

It is improbable that there were many relapses later than those discovered; and as several of the cases had only eight or nine doses instead of twelve, it seems likely that less than 36 grains may be effective.

It is advisable to keep cases under observation for not less than fourteen days after treatment, and to examine them not less than four times during that period if relapses are to be detected.

The drug is without appreciable effect upon the intestinal flagellates, but has an effect, usually temporary, on *Entamoeba coli*.

Treatment of *Entamoeba Histolytica*. In a study of the patients with protozoal infections at the Walton hospital in England, Clifford Dobell¹ found infected patients as follows:

Number of men infected with—

<i>Entamoeba histolytica</i>	22 = 11 %
<i>Entamoeba coli</i>	84 = 40.9 %
<i>Giardia</i> (= <i>Lambia</i>) <i>intestinalis</i>	40 = 19.5 %
<i>Chilomastix</i> (= <i>Tetramitus</i>) <i>mesnili</i>	16 = 7.8 %
<i>Trichomonas hominis</i>	5 = 2.4 %
<i>Isospora</i> sp.	1 = 0.48 %

The treatment first employed was emetine hydrochloride given hypodermically. Each man received from 11 to 14 grains in daily doses of 1 grain. Following this

(1) Brit. Med. Jour., Nov. 4, 1916.

treatment the stools were carefully examined by the author for a sufficient time to determine whether or not the patients could be classed as cured. It was found that fourteen of the twenty-one patients first treated this way continued to discharge the entamebas and cysts in the stools.

In a second group, patients were given the double iodide of emetine and bismuth in 1 grain doses, three times daily, after meals until 36 grains had been given. This removed the organisms and cysts from the stools entirely. This treatment had such good effects upon both those who had been given the emetine hydrochloride and those who had not. The only untoward effect of the drug was that it produced nausea and sometimes vomiting, but by giving it on a full stomach this difficulty was largely overcome.

Dobell states that the effects of the administration of the double iodide upon the protozoal content of the stools—which are the effects that have especially come under his own observation—are truly remarkable. Within four days of the commencement of treatment all stages of *Entamoeba histolytica*, whether amebas or cysts, have completely vanished from the feces, and in no single instance have they been subsequently found.

Many of the men treated with the double iodide were infected with *Entamoeba coli*, *Lambli*a and *Chilomastix*, and in no case has the treatment removed any of these protozoa. As a rule *E. coli* disappears from the feces during treatment, but it almost invariably reappears afterward. *Lambli*a and *Chilomastix* are quite unaffected by the double iodide, though the diarrhea produced by the drug often causes the appearance of the free flagellates, in addition to the cysts, of these forms in the feces.

“It seems, therefore, that in emetine bismuth iodide we have a specific drug which, while unpleasant to the patient, is very deadly to *E. histolytica*, but harmless to the other protozoa of the human bowel.”

A series of 224 instances of protozoal infections were studied by Margaret W. Jepps.² Eleven of the patients had infections of *Entamoeba histolytica* alone and twenty-

(2) Brit. Med. Jour., Nov. 4, 1916.

one had this organism in conjunction with other parasites. The treatment consisted of injections of emetine hydrochloride hypodermically in 1-grain doses on successive days until at least 10 grains had been given. It was found that twelve of twenty-one patients were certainly not permanently freed from *Entamoeba histolytica*. Most of the patients treated had periods during which the organisms were absent from the feces following the treatment. There was a good deal of variation in the time elapsing before the disappearance and reappearance of the cysts in the stools. The interval before the detection of the latter must be kept in mind when fixing the criterion for discharge as cured. The time between the end of treatment and the discovery of cysts in the stools again varied from five to twenty days. While the results obtained in this work are somewhat better than those given by Dobell, they are far from satisfactory and, indeed, constitute further evidence in favor of the double iodide treatment to replace emetine.

Progress in Knowledge of Dysentery. An editorial in the British Medical Journal³ contains some valuable references and points of information concerning the work that has been done on dysentery, and although it mentions the work of Dobell,⁴ it seems fair to quote the opinion. The editorial states:

"The acute dysentery of war has generally been regarded as in the main bacillary, and this was certainly true in the South African war (1899-1902), though in the Spanish-American war the American troops in Manila, where amebic dysentery is endemic, suffered from both forms, and, as Strong proved, mixed infections occurred. When cases of dysentery contracted in Gallipoli by the Mediterranean Expeditionary Force began to arrive in this country during the autumn of 1915 difficulty in deciding as to their nature, and therefore on the appropriate treatment, arose. For whereas at the front, and especially in the base hospitals at Alexandria and Cairo where amebic dysentery is common, the prevailing opinion was in favor of the amebic origin,

(3) Brit. Med. Jour., June 2, 1917.

(4) Pages 109-110, this volume.

in this country evidence in support of this view was commonly wanting. This divergence of opinion may reasonably be explained, at least in part, by the convalescent state of the patients, who had nearly all received routine treatment by emetine before their arrival here. Subsequently the question was apparently settled by the compromise that both forms occurred, that each was predominant at different periods, and that mixed infections were frequent.

"Among the valuable reports now being made on the subject of dysentery to the Medical Research Committee special interest attaches to that of Dr. Bartlett 'On Dysentery in the Mediterranean Expeditionary Force,'"⁵ based on the experience of some eight months' work as pathologist to No. 21 General Hospital in Egypt, where he examined 1,129 stools and observed 61 necropsies on cases of dysenteric ulceration, the microscopic examination of the material being completed at the London Hospital. This careful and elaborate research confirms the opinion that the dysentery was primarily amebic. Secondary bacterial infection, however, was very frequent, and in some cases so intense as to obscure the amebic lesions by a diphtheroid inflammation resembling that of bacillary dysentery. Out of the sixty-one necropsies, fifty-six (92 per cent.) showed amebic lesions, and out of the five remaining cases, tentatively called pure bacillary dysentery, evidence of a specific infection by organisms of the dysenteric group was forthcoming in one only. Examination of 477 dysenteric stools showed that 379 (79.4 per cent.) contained vegetative amebas of pathogenic type. From these results it is obvious that specific treatment should be adopted as soon as possible so as to arrest amebic ulceration before the colon has become more vulnerable to bacterial invasion. Thus Sir Ronald Ross' advice in August, 1915, that emetine should be given early to all cases of dysentery was fully justified, and was considered to have prevented a much higher mortality among the forces. But as secondary bacterial invasion may prove fatal from purulent diarrhea after amebiasis has been removed by emetine, measures to combat it are necessary,

(5) Pages 99-104, this volume.

and for this purpose saline purgatives to flush out the colon and bismuth mixture by the mouth were employed. A powerful multivalent anti-dysenteric serum, prepared at Alexandria, was also used in such cases, but opinions as to its value varied widely.

"The cases referred to by Dr. Bartlett received injections of emetine hydrochloride $\frac{1}{2}$ grain until 6 or 10 grains had been given, and after an interval one or two further short courses. Usually this was successful, but it is frankly admitted that in some instances a thorough course of treatment failed to eliminate amebiasis. The high reputation of emetine injections to *Entamoeba histolytica* carriers has been gravely impugned by Mr. Clifford Dobell,⁶ who states that full courses (10 to 12 grains or more) are successful in about one-third only of the cases treated, and that subsequent courses offer little hope of cure. He advocates the oral administration of emetine bismuth iodide in daily doses of 3 to 4 grains until 36 to 40 grains have been given. By this means the vast majority (90 per cent.) of carriers are cured even when emetine injections have previously failed. Dr. G. C. Low, in a further report to the Medical Research Committee, mentions that vomiting caused by the administration of emetine bismuth iodide can be eliminated or reduced to trivial proportions by giving the double iodide in pills coated with salol, as recommended by Dr. H. H. Dale.

Ipecac in Dysentery. In this article on recent experience with ipecac and its alkaloids in the treatment of amebiasis Sidney K. Simon,⁷ of New Orleans, recalls the use first of ipecac itself in the treatment of this disease and the apparent excellent clinical results obtained by it. He also refers to the use of one of the alkaloids of ipecac, emetine, which has been used for the same purpose for about four years. This alkaloidal principle extracted from the ipecac root, when given in small doses, from $\frac{1}{2}$ to $1\frac{1}{2}$ grains a day, has also been found to remove from the stools of patients suffering with amebiasis larger numbers or all of the organisms within a very short time after the treatment is instituted. Many

(6) Pages 99-110, this volume.

(7) New Orleans Med. and Surg. Jour., December, 1916.

extensive claims for the value of this drug have been made, and the author says that the question which now presents itself for consideration is whether the early claims made in behalf of emetine as an amebicidal agent superior in value to ipecac itself has been sufficiently justified. Further, it is said that from a culling of the recent literature there would seem to be increasing evidence of doubt upon that score.

The use of emetine instead of ipecac was of value in disposing of the irritating effects of the latter on the mucus membrane of the stomach, and while it was found to produce results that were apparently as good as those produced by the administration of ipecac itself, it has also been found that it does not prevent recurrence of the disease.

It is with the prevention of relapses, a sequel so characteristic of protozoan diseases, that the real effectiveness of these drugs should be judged and their relative merits established. In this respect it would seem that ipecac possesses a far greater value than emetine itself.

The cause of relapses in amebiasis, as in other infections due to protozoa, may be traced to the tendency which the animal organisms exhibit to pass from the active vegetative state to a quiescent condition with the formation of cysts. It is the inability of ipecac and especially of emetine to destroy the organisms in the encysted form that leads to, or rather allows the relapse of amebiasis, and therefore renders the drug less valuable than its clinical effects would indicate.

In 1894, Paul and Crownley showed that the root of ipecac consisted, in fact, of two distinctly active alkaloids, to which they gave the names emetine, and cephaline. The physiologic and toxic action of these two alkaloids on the human organism, as well as on some of the lower animals, was tested by Wild and found to produce, to a great extent, effects similar in character.

Emetine, however, is the one of these two alkaloids that has been used in the treatment of amebiasis with a few exceptions.

Leonard Rogers reported in Bengal in 1914 some observations of the use of cephaline in the treatment of

this disease. Simon has used it in the treatment of a few cases and reports the following observation:

Cephaline would seem to possess an amebicidal action upon the free living entameba to a degree equal to that of emetine in the same dosage.

The destructive effect of cephaline on the encysted organism would appear to afford more promise of success than that induced by emetine. In one of the cases cited the patient remained free from relapse for a period of five months with no reappearance of the cysts in the stool during that time after repeated examinations.

The administration of cephaline by the sub-cutaneous route produces considerably more irritation and pain at the site of puncture than does emetine.

Evidences of gastric disturbances accompanied by nausea and vomiting are encountered with more frequency and to a greater degree with the use of cephaline than with emetine.

There is less tendency to diarrhea in the course of the cephaline therapy than following the use of emetine.

The employment of a combination of the two alkaloïds by hypodermic injection would seem to promise a greater amebicidal effect than is obtained with emetine alone.

No evidence of toxemia was observed following the employment of the comparatively small doses of cephaline.

It has already been noted in this article that instances have been observed in which a severely toxic effect, in one instance fatal effect, of emetine has been observed. In each of these instances the drug had been employed in subcutaneous doses of from 1 to 1½ grains a day over a considerable length of time—in the fatal case, over a period of twenty-nine days.

In a consideration of the treatment of intestinal amebiasis, with special reference to ipecac and its derivatives, B. C. Crowell,⁸ of the University of the Philippines, College of Medicine and Surgery, discusses at considerable length several phases of amebic dysentery.

Of most importance, however, is his reference to a new method of treatment which promises, in his esti-

(8) Jour. Amer. Med. Ass'n., July 7, 1917.

mation, more favorable results than have been obtained heretofore. He refers to Du Mez, who in 1915, published a formula for two drugs which he suggested might be of value in treatment of amebiasis. These preparations were devised by Du Mez especially for the treatment of this disease, hoping to obtain a drug which might be given by mouth, which would be efficacious, and which would not have the drawbacks ascribed to previous forms of treatment of the disease. These salts were emetine mercuric iodide and emetine bismuthous iodide.

As a result of his experiments on dogs, Du Mez says that these two compounds may be given in doses representing, 0.03 grams of emetine hydrochloride without causing vomiting and without any apparent nausea. The latter of these preparations alone has demanded attention. It has the useful property of being practically insoluble in dilute acids, but soluble with comparative ease in weak alkali. It might be expected therefore to pass the stomach unaltered and then being dissolved in the alkaline juices of the duodenum, to undergo decomposition as it passed along the bowels with liberation of emetine and precipitation of bismuth sulphide. It is said that no serious attention was paid to this suggestion, until Dale, in July, 1916, reported some results from its use. He tried it in ten cases with good results in eight. The formula of Du Mez is given as follows:

TABLE 1.—DU MEZ FORMULAS.

Emetine Mercuric Iodide.

Iodine	43.08 per cent.
Mercury	12.50 per cent.
Hydrogen (as hydrogen iodide).....	0.23 per cent.
Emetine	44.19 per cent.

Emetine Bismuthous Iodide.

Iodine	58.26 per cent.
Bismuth	12.36 per cent.
Hydrogen (as hydrogen iodide).....	0.30 per cent.
Emetine	29.08 per cent.

The results of a large number of workers and authors, who have used emetine and ipecac and their derivatives in the treatment of dysentery are quoted.

In the conclusion the chief item of the article emphasized is that Du Mez, in Manila, first suggested the

advantageous use of his two compounds in the treatment of amebic dysentery, and thus far only the British workers get the credit for having tried one of them.

Treatment of Amebic Dysentery. The statements made in this article by John Pelham Bates⁹ are said to be based upon experiences obtained during a period of nine years' work in the Panama Canal Zone, ending in 1913. The chief factor that has interested the author in the preparation of this paper has been the presence in recent literature of articles dealing with recurrent cases of this disease. He says that from his own experience since the revival of the use of ipecac it appears that the recurrences ought not to take place, if all of the problems entering into the treatment of amebic dysentery are considered and the treatment necessary to meet these problems is carried out; that is, treatment to aid the action of ipecac as an amebicide, treatment to hasten the complete healing of the ulcerations in the intestine and the allowing of ample time for these ulcerations to heal entirely before patients are discharged as well; in short, a coöperative or correlative treatment to ipecac.

Concerning the active treatment, he says that one of the first and most necessary factors in treatment, whether the case is mild or severe, is complete rest. The patient is put to bed and given a saline purge or castor oil. He is kept in bed until all the acute symptoms have subsided. After the purgative has acted, emetine or ipecac is begun. One-half grain injections of emetine daily are used for an adult until 2 grains are given; the dose is then increased to 1 grain a day and continued until all amebas are cleared from the stool, as shown by microscopic examination. This will usually require a total of from 5 to 6 grains of emetine. If one does not have access to the microscope, it is well to give a total of at least 6 grains of emetine. At this time the emetine is discontinued, and bismuth subnitrate in large doses is begun. Bismuth acts in two ways: first, as a sedative on the intestinal tract and as an aid toward the healing of the ulcers present; second, as was first pointed out by Deeks, bismuth itself acts as an amebicide and is an added help in destroying such amebas as may be left

(9) Jour. Amer. Med. Ass'n., July 29, 1916.

after the discontinuation of the emetine or those that may be formed from the "encysted" stage. Bismuth is usually given in 1-dram doses every four hours during the waking hours until the stools are well formed, and until some constipation is present. It may then be reduced to 1 dram three times a day until the patient is discharged as well.

Enemas of normal saline solution, 2 or 3 quarts at a time, are begun as soon as the effect of the salts or castor oil has subsided, and are used every four hours during the waking hours, and continued in this quantity throughout the entire period of the administration of ipecac or emetine. They may then be reduced to two or three a day and later to one a day, merely to prevent the constipation following the bismuth. It is well to remember that in flushing the bowel it is necessary to use a short tube in order to avoid the ulcers that may be low in the rectum. At first it will be found that the bowel will tolerate only a small quantity of fluid; it finally becomes more tolerant, and a quart or more will easily be retained. In attempting to examine stools for amebas after these large enemas, it will be necessary to retain the whole stool, that is, the enema and such fecal matter as may be present. Out of this one should select particles of mucus, shreds of necrotic tissue, or flecks of bloody material, and at least six or more separate examinations of this material should be made before one concludes that the stools are negative for amebas.

Experience has shown that sweet milk is the best food in amebic dysentery. It may be given every two hours during the day in quantities of from 4 to 8 ounces at each feeding. After the more acute symptoms have passed and the stools are beginning to be partly formed, the milk may be gradually increased in amount and the time between the meals lengthened. At this stage eggs, soft-boiled or poached, may be added to the diet with one slice of dry toast at each feeding. As the improvement continues, the food may be gradually increased until the patient is finally returned to a full diet.

To carry out this management until one is reasonably sure that all ulcers are healed and replaced by new tissue will require in the acute cases at least four weeks'

time. In the more severe cases it will require a total of from six to eight weeks before one should feel safe in discharging the patient as well.

Serotherapy of Bacillary Dysentery. The treatment given to dysentery patients by J. B. Fisher¹⁰ is dietetic, medicinal, and specific.

Patients are only allowed albumin water, barley and lemon water for the first forty-eight hours. Coincidentally with the improvement of the general conditions the diet is gradually increased. Milk is not allowed except in the form of pudding or custard. One dram of magnesium sulphate is given three times a day for the first few days, and then, as the stools diminish in frequency and improve in appearance, the amount is gradually reduced. This applies to practically all cases. Rectal lavage with 1 : 1,000 solution of copper sulphate, and *mistura simaruba* often benefit more chronic cases. Reliance is placed by Fisher on specific treatment, namely, multivalent antidysenteric serum. Each individual case must be judged on its merits. In the more severe cases Fisher injects 80 c.c. into the flank within a few hours of admission, but generally leaves the milder ones until the following morning, and then may give 40 or 60 c.c. One large dose of serum, he asserts, is sufficient to effect a cure in some cases; other patients, though much improved, require more, and in these, after waiting forty-eight hours, Fisher gives a further 60 or 80 c.c. A few of the worst may need a third or even a fourth dose. In cases of the fulminating variety, the patients have been given 140 or 160 c.c. intravenously within twenty-four hours of admission. If four doses of 80 c.c. each, spread over a period of six or seven days, have not brought about the desired result, further injections are indicated.

The results have convinced G. A. Finlayson² that 100 c.c. antidysenteric serum should be given intravenously without delay, followed, if necessary, by a second dose within twenty-four hours. After one intravenous injection of 100 c.c., subsequent doses may be injected subcutaneously, he says, into the axilla, infra-

(10) Brit. Med. Jour., Jan. 13, 1917, p. 43.

(2) Ibid., p. 46.

clavicular space, or flank. The amount which Finlayson usually gives is 40 c.c. in the morning or evening. In association, a mixture containing 1 dram of magnesium sulphate, 1 dram of sodium sulphate to half an ounce of water, or 1 ounce of *mistura alba* is administered hourly, or even more frequently, until the motions become pale and watery, containing perhaps a few bloodstained shreds; the interval between the doses is then lengthened according to the conditions noted. The diet in the early stage is restricted to albumin water and barley water, with strained chicken tea and meat juices.

Treatment of Dysentery in India. The form of treatment carried out by T. J. Carey Evans¹ in the care of soldiers suffering from dysentery in India is outlined as follows:

In all cases of acute dysentery coming into the hospital the patients were given 2 drams of magnesium sulphate every two hours until the stools became feculent or until two ounces had been given. This was done as a routine measure unless the dysentery was of the amebic type. This method of treatment with rest and diet proved, in the author's experience, most satisfactory. If there were no improvements from this, the patient was given bismuth salicylate and salol, āā, 10 grains three times daily for three or four days and at the end of this time went through a course of magnesium sulphate treatment. This salt acts mechanically, Evans says, by ridding the patient of the bacterial and other débris in the intestinal canal, and possibly also by virtue of its lymphagogic action may draw into the intestinal canal any antitoxins that may have been formed in the patient's blood. With this treatment in the field ambulance, it was found possible to return to duty within 14 days 90 per cent. of the cases of dysentery which occurred among the Indian troops.

Should the patient have intense pain, hot fomentations applied to the lower part of the abdomen frequently relieved it; otherwise 10 minims of camphorodyne or 10 grains of Dover's powder were found to act satisfactorily. The promiscuous injection of emetine in every

(1) Brit. Med. Jour., March 31, 1917.

case of dysentery he says is distinctly harmful. The results are very disappointing and one's faith in the specific action of the drug is apt to be shaken. Emetine should be used only in cases that are distinctly amebic in type, or in those in which the entameba has been discovered in the stools. Emetine was found to have little effect in cases of mixed dysentery until the patient had gone through a course of the saline treatment first, when it has the same marvelous action as one observes in India in cases of simple amebic dysentery. The injection of emetine should not be done indiscriminately, and the results of each injection should be carefully observed. In suitable cases 1 grain should be injected subcutaneously night and morning. If no good results occur after four injections it should be stopped on account of the depressing influence it exerts. It can be resumed after a few days' interval if thought necessary.

Amebic Dysentery in Morocco. A. Mauté² lays great stress on two things: First, that the disease is a chronic affection in which the dysenteric crisis is only an incident; second, that when the stools again become normal the patient is not necessarily cured.

In order to determine the absence of cysts in the stools, a provocative rectal injection of 1/10 per cent. iodine-potassio-iodide solution is given in the morning. In two or three hours the stools are examined for cysts. It is surprising how often the parasite will appear, although there may be no objective symptoms. The disease is the more to be dreaded in that it often appears so light that the patient neglects to seek medical advice. Every intestinal derangement, however slight, ought to be placed under suspicion and repeated examinations made of the stools.

The author notes that the presence of other intestinal parasites seems to increase the resistance of the amebas. The association with trichomonas always predicts a case rebellious to treatment. These latter are to be removed with turpentine.

How long the disease lasts is not certainly known; one can always obtain a history of some previous intestinal trouble. Emetine hydrochloride is a specific in the dys-

(2) *Presse méd.*, Oct. 26, 1916.

enteric crisis, this author states, in doses of 8 cm. twice in 24 hours for the first three or four days; then 4 cm. for three or four days following. By this time the dysenteric phase is over. If diarrhea continues, an explanation will often be found by searching for other protozoan parasites or worms. After six days of no medication another series of five injections of 4 cm. is commenced. After a week of no medication another series is given and still one other series. If no cysts are found after the iodine irrigation the patient is pronounced cured and isolation ceases. As a matter of precaution, the author would have patients return after six or eight weeks for a final course of treatment.

Arsenobenzol was found far less effective than emetine in treating dysenteric crises, but is employed in conjunction with emetine in very chronic and rebellious cases.

An Epidemic of Bacillary Dysentery in 1915 at Guercif in Eastern Morocco. During this epidemic Gabriel Boudet³ had about 300 cases under observation, and the chief points of interest in the article are the methods of propagation and the methods of treatment. Concerning the former it was conclusively shown that drinking water had nothing to do with the spread of the epidemic, although the water supply was very poor from a sanitary viewpoint. This is especially interesting, since there were numerous military posts separated from one another by short intervals, yet all having the same water supply. The epidemic visited only certain of these posts. In each instance the introduction of the disease into these isolated posts was traced to some carrier from without, either some one in apparent health or ill with the disease. The spread of the disease by direct contact was especially shown by the case of the nurses, among whom infection was extremely common. In the propagation of the disease the feces themselves are by far the most important agent; flies, dust and other agents are only secondary. On account of the great invalidation dysentery entails, it seems advisable to isolate all patients with any diarrhea whatever, rather than

(3) Presse méd., June 29, 1916.

risk an epidemic, likewise the night cans ought to be eliminated from the troop streets.

In the matter of treatment, diet is of the greatest importance and is sufficient without any other medication in the majority of cases. The author prefers in the matter of diet to give his patients only vegetable broth [*bouillon de légumes*] for the first four or five days and then when the stools are down to two or three a day he adds purée of potatoes; meat he allows only after the stools are normal.

Owing to the shortage of anti-dysenteric serum, only fifty-six patients were treated with it, and these were the worst cases. Of the other remedies, the author found Segond's Pills of great value.

Segond's Pill:

R	Powdered ipecac	0 05
	Calomel	0 02
	Extract of opium.....	0 01
	White honey	Q.S.

One Pill.

Dose: From 6 to 10 a day.

The patient is placed on a diet and on the first day receives 15 gm. of sulphate of soda; during the second and third days he receives 10 gm. each and then 6 Segond's pills. As the stools decrease, the number of pills administered is diminished. One hundred and fifty cases treated in this way showed an average duration of sickness of 22.5 days. The severe cases treated by serum (first injection 60 c.c.) showed an average duration of 24.5 days, thus demonstrating the superiority of serum treatment, since these cases were the worst.

The author has seen cases treated by intestinal lavage with hydrogen peroxide and permanganate of potash, but has seen no real results from it.

Chronic Amebiasis in France at the End of 1916. P. Ravaut⁴ shows the ever increasing importance of this disease in the French Army both on account of the invalidation it causes and on account of the failure of the army surgeons to recognize it, with the result that

(4) Presse méd., Feb. 8, 1917.

patients with a diagnosis of "gastro-enteritis with anemia," of "chronic enteritis with asthenia" or "diarrhea with rheumatism" remain in the ranks as foci of infection. The disease was originally brought into France by territorials from Africa and elsewhere and now seems well established in certain regions. The essentially gradual onset and chronic course makes it especially liable to be overlooked. The author prefers to call the disease "amebiasis" rather than "amebic dysentery," since this dysentery feature is so often absent.

In the words of the author, the symptoms as encountered in the French army are as follows: "Chronic amebiasis may follow upon a dysenteric crisis, but most commonly the initial symptoms are indefinite; for a day or so the stools are glairy and bloody, then become diarrheal and the disease is gradually established. Again, there may be no special symptoms save an abnormal number of stools (from 4 to 10) Palpation of the abdomen discloses a tenderness of the large intestine. . . . The stools are habitually soft, pasty, and like cow dung . . . are very abundant. Sometimes there are glairy outbursts streaked with blood, especially caused by cold or fatigue. . . . The diagnosis of amebiasis is generally easy, if one only thinks of it."

Besides these symptoms, the author speaks of another common complaint which has often led to the erroneous diagnosis of "rheumatism," and this is pain in the bones. The association of these osseous pains with amebiasis is shown by their coincidence with exacerbations of the intestinal disorder; they are relieved by anti-amebic treatment, but not by salicylates. Besides they are distinctly osseous, not articular.

Regarding diagnosis, the author lays stress upon the search for amebic cysts.

Treatment consists of the usual combination of arsenic and emetine.

First Cases of Tropical Dysentery in Spain. Acting on the suspicion, prevalent among medical men for some time, that amebic dysentery is endemic in Spain, especially on the eastern littoral, F. Martinez⁵ made a careful investigation to determine the truth of this, and in

(5) Presse méd., June 29, 1916.

this article presents the history of three cases which he thinks support the proposition that amebic dysentery is endemic on the eastern littoral. In each of the cases the subject had always lived in the same place and had never been in contact with foreigners. Diagnoses were made by demonstrating the parasites in the stools and by positive inoculations on cats.

Amebic Dysentery in Missouri. A record of eight patients suffering from amebic dysentery, which is said to be endemic in the region of St. Louis, is published by Joseph W. Larimore⁶ of the Washington University Medical School. The author states that the presence of these cases raises the question of whether or not the disease may not be becoming more common locally. They were found among approximately 1,000 cases at the Gastro-Intestinal Clinic, of the Washington University Dispensary, during fifteen months. Larimore says that perhaps the discovery of these cases is merely because of a more diligent search for an etiologic factor in a diarrhea and colitis symptom-complex. However, in several of these cases a search was unnecessary. The diagnosis could be strongly suspected from the history.

In a number of cases reported here, the geography of the individual case is absolutely restricted to St. Louis or at most to the state of Missouri. The author says that this must mean either that the disease has gained a foothold in this community, or that these persons were infected with imported foods.

The treatment of the case was limited to the use of ipecac and emetine preparations, to moderate dietetic restrictions and to the symptomatic relief of local rectal conditions. The aluminum silicate and ipecac tablets were used, also the injections of emetine hydrochloride subcutaneously and intramuscularly. The injections in all cases produced more or less local soreness. Later the author adopted the intravenous method of administration, using 1-grain doses. The avoidance of the soreness caused by the subcutaneous or intramuscular injections was found to be a great relief to the patient. It was also evident that the drug is more effective by intra-

(6) Interstate Med. Jour., September, 1916.

venous injection, perhaps reaching the tissue in greater concentration.

In a discussion of the results he states that one patient who relapsed promptly at no time afterward gave full symptomatic response to intravenous emetine therapy. The suggestion is made that the amebas may have become emetine fast. One patient giving definite symptoms of hepatic abscess improved promptly with intravenous administration of fourteen 1-gr. doses, and relapsed with ulcerative proctitis after four months. The author says that the value of emetine therapy by oral or by parenteral administration was demonstrated by the prompt relief of all symptoms and by the rapid and complete healing of the visible intestinal lesions. The tendency to relapse may be explained by a residuum of infection, which was allowed when either method of administration is used alone.

The conclusions drawn are that the presence of these cases of entamebiasis among approximately 1,000 unselected gastro-intestinal patients suggests its greater frequency in St. Louis and vicinity than is generally considered; also, that emetine has a direct and curative action upon the lesions of entamebiasis, but when used by either oral or parenteral administration, it fails to eradicate the infection.

Special Manifestations of Dysentery. In a recently observed extensive epidemic of dysentery, with absence of amebas and dysentery bacilli, but with frequent presence of a paracolon organism, O. Cronzon⁷ states that rheumatic manifestations and conjunctivitis were so striking as complications as to lead finally to a systematic inquiry for diarrhea where the patient, in the combined presence of the two conditions, failed to complain of it. Dysenteric rheumatism has long been known, having been described even by Trousseau. In the present series of cases the knees, tibio-tarsal joints, and sometimes the elbows and shoulders were the articulations affected. Effusion sometimes lasted several weeks and led to muscular atrophy. Conjunctivitis, however, is a complication not hitherto described. It may appear

(7) Bull. et mém. de la Soc. méd. des hôp. de Paris, Dec. 7, 1916.

either before or after the rheumatism, or be present without it. In the latter case it appears at the close of the tenth day of dysentery; when associated with rheumatism—generally in the most severe dysentery cases—it appears about the fifteenth day. The conjunctivitis is not due to infection by the hands, as it is bilateral from the start, does not awaken any mucopurulent discharge, and seems always negative bacteriologically. It involves especially the conjunctiva of the lower lid, and passes off completely, without treatment, in six to ten days. Only four cases of isolated conjunctivitis were observed, but many slight cases occurred. In but one case were keratitis and iritis superadded. The condition appears to be a rheumatic or metastatic conjunctivitis similar to the conjunctivitis of simple acute rheumatism, of which the author has recently seen two cases, or to the metastatic conjunctivitis of gonococcus rheumatism recognized by Christmas, Wassermann and Morax. Knowledge of conjunctivitis and rheumatism as manifestations of dysentery is manifestly of importance for the detection of "*fruste*," germ-carrying cases of this disease and the early institution of prophylactic measures.

RAT-BITE FEVER.

French Cases of Sodoku, a Toxic Infection Caused by Rat Bite. H. Roger^s takes up in great detail the cases of rat-bite disease which have been reported in France. Out of seven cases he finds but two that approach the classical type. In two cases there was lacking the characteristic eruption. In one case the inflammatory recrudescence at the wound was absent, nor was there lymphangitis or adenitis; besides the period of incubation was only four days. In another, the incubation was only three days and showed nothing except a febrile disturbance.

Roger reviews the opinions of Japanese observers:

According to Misoguchi there are four clinical forms of the disease.

(8) Presse méd., April 5, 1917.

1. A type with preponderance of local symptoms: infection, gangrene, edema of the wound, and local or general eruption.

2. A febrile type with intermittent and remittent fever combined with a general exanthem.

3. A painful type which starts with pains and then follows the above.

4. A nervous type with predominance of motor and sensory disturbances (paresthesia, paresis, diminution of reflexes) and exanthem.

According to Miyaki there are three types, depending on the fever curve.

1. Febrile type with exanthem—most common.

2. A febrile type with predominance of nerve symptoms.

3. An abortive type characterized by one or two febrile attacks and no exanthem.

In conclusion Roger remarks that the causal agent is still to be discovered.

TETANUS.

Treatment of Tetanus. Twenty-five cases of tetanus are reviewed by H. R. Dean.¹ All the patients had suppurating wounds, but in the majority the wounds were not more serious nor had the suppuration been more serious than in the average patient sent home to a hospital.

In four cases the wounds were of a comparatively trivial nature. In nine cases the wounds at the time of the onset of tetanus had completely or almost completely healed. Dean states that if every wounded soldier, irrespective of the size or condition of the wound, were given a prophylactic injection on his arrival at home there would in all probability be a still further reduction in the number and severity of cases of tetanus.

Compound fractures are a particular source of danger, and were present in eleven of twenty-five cases of tetanus. In three of the twenty-five cases the

(1) *Lancet*, May 5, 1917.

disease ran an extremely short and mild course. These were the only three patients who had received a prophylactic injection after their arrival in England. One result of prophylactic injection is to prolong enormously the incubation period, with the result that tetanus may occur after the wounds have completely healed, and the patient has been transferred to a convalescent hospital. Under these circumstances the earliest signs are readily overlooked. The pain associated with the early and local symptoms may lead to a diagnosis of rheumatism or muscular rheumatism.

The earliest signs may consist of clonic or tonic contraction of muscles in the immediate neighborhood of a wound, usually in the nearest flexor group. The signs may remain localized for many days, and it is characteristic of some cases occurring in inoculated patients that the period of onset is enormously prolonged. After a longer or shorter interval generalization occurs. The muscles of the jaw, neck and abdomen become stiff. There is profuse perspiration and the reflexes of the lower limbs are exaggerated. In many cases the pulse-rate may be very rapid and the temperature normal. On the other hand, even in inoculated persons and after a very long incubation period, the disease may begin suddenly with spasm of the muscles of the jaw and neck.

Of five mild cases treated by intramuscular and subcutaneous injections of serum all five patients recovered. Of fourteen patients treated chiefly by intravenous injections thirteen recovered. Of five treated by intrathecal with or without other injections three recovered. One patient who was given an intravenous and subsequently an intrathecal injection died. If the signs are well localized and are not spreading rapidly, Dean says, intramuscular injections afford an adequate method of treatment. In severe cases, and in those in which signs are generalized, an intravenous injection (30,000 units) under deep chloroform anesthesia should be given. After such injection the further progress of the disease is usually arrested, and definite improvement may be expected two to seven days later.

The essential principle of serum treatment, in Dean's

opinion, is to give a very large dose of antitoxin at the earliest possible moment. This object can be most easily attained by the intravenous route. In four cases serum treatment was confined to a single intravenous dose of 30,000 units. In three other cases no serum was given subsequent to the intravenous injection. In these seven cases recovery was as rapid as in six other cases in which subsequent injections were given. The serum of patients was shown to contain free antitoxin at various intervals up to thirty-nine days after an intravenous injection of 30,000 units.

Animal Experiments with Tetanus Antitoxin.

Experiments conducted by D. Bruce² on monkeys exhibit the effect of a single injection of antitetanus serum on a single precurrent dose of tetanus toxin and show a difference between the results obtained by the intramuscular and intrathecal methods respectively.

The contrast seems sufficiently marked to be significant, Bruce thinks, although the experiments are at present few in number. The results are distinctly in favor of the efficacy of the intrathecal as against the intramuscular method in his opinion.

The results obtained by F. Golla³ in a series of animal experiments seem to show the indubitable superiority of the intravenous and intrathecal routes over the subcutaneous. Such superiority is attributed by the author to the slow absorption of tetanus antitoxin injected subcutaneously.

KALA-AZAR.

Treatment of Kala-Azar. The successful treatment of six cases of kala-azar in Europeans by intravenous administration of tartar emetic was reported by Sir Leonard Rogers,⁴ in February, 1915. The same author now gives a record of treatment of twelve cases by the same management. Detailed histories of each of these patients during their treatment and following the time they were sent away from the hospital are given in the article;

(2) Lancet, May 5, 1917.

(3) Ibid.

(4) Lancet, May 5, 1917.

an extensive table containing data before and after treatment is also presented.

The treatment consisted in giving intravenously a 2 per cent. solution of tartar emetic. The only changes made after the treatment of the first series of six patients was to increase the dose more rapidly than was done at first. It is now recommended that in adults one should begin with 4 c.c. of the 2 per cent. solution of tartar emetic, and add 2 c.c. at the second injection, and if no toxic symptoms occur, 1 c.c. from that point to 8 or 10 c.c., above which it is not necessary to go. If toxic symptoms arise, other than cough, immediately after the injection, the dose should be reduced until no sickness or nausea occurs, as body-weight may be lost as a result of repeated sickness from too large doses. The earlier doses may be given every other day, but when the full dose which is well tolerated is found one injection every three days suffices.

Of the toxic symptoms, nausea is the most important sign, and its occurrence is an indication for reducing the dose. No serious symptoms have resulted from the large doses given in this series of cases, unless the fainting fits in one individual were predisposed to by the drug. Cough just after the injection is common but unimportant. In patients with dropsy or albumin in the urine the dose should be increased cautiously.

The treatment is continued for from several weeks to two or three months after the fever ceases, and only stops, as a rule, when the body-weight has much increased, when the spleen has become considerably reduced, when the blood has approached or reached the normal as regards both the red and the white corpuscles, and when the parasites have disappeared from the spleen. This precaution was adopted in view of the great chronicity of sporadic kala-azar, and it has been fully justified by the fact that none of the cases followed up for from several months to a year after leaving hospital relapsed, while most of the patients were doing full work at the time this report was made.

Before the institution of this form of treatment of kala-azar, the marked fatality was quoted in various places authentically as being from 78 to 96 per cent. The

plan of segregation of those ill with this disease suggested by the author has worked well prophylactically, but the active treatment by intravenous injections of tartar emetic has worked wonders in reducing the mortality from such high figures to practically nothing.

BERIBERI.

Relation of Diet to Beriberi and Our Present Knowledge of the Vitamins. This subject is discussed at some length by E. B. Vedder,⁵ of the Medical Corps of the U. S. Army.

At the present day, he says, there is a general consensus of opinion to the effect that beriberi is caused by a dietary deficiency, or that it is a disease resulting from faulty metabolism, and is directly caused by the deficiency of certain accessory food substances that have been called vitamins.⁶ In a general way this opinion is based on the following facts:

1. The complete failure of the adherents of the infection and intoxication theories to prove their case.

2. The carefully planned and controlled human feeding experiment of Fraser and Stanton, in which they demonstrated beyond all cavil that beriberi can be experimentally produced in men by too exclusive feeding on over-milled or highly polished rice. This experiment was later repeated by Strong and Crowell in the Philippines with a similar result.

3. The long series of animal experiments which have been repeated with substantially the same results in all parts of the world and by which it has been equally demonstrated that various animals, but particularly birds, when fed on diets that will produce beriberi in man suffer with a disease which in some instances is identical in symptomatology and pathology with human beriberi, and in other instances is so similar that we must believe that it is essentially the same disease.

4. The instances in which beriberi has been eradicated from various institutions or groups of men by certain simple but radical changes in the dietary.

(5) Jour. Amer. Med. Ass'n., Nov. 18, 1916.

(6) See also page 186, this volume.

Every sanitarian should be familiar with the practical results of this character reported by Van Leent, Vorderman, Takaki, Fletcher, Highet, Heiser, Theze, Chamberlain and others.

Vedder discusses the relation of vitamins to metabolism and then says:

“Much criticism has been expended on the term ‘vitamin.’ Most of this criticism is from chemists who point out that the termination ‘amin’ indicates a definite chemical structure and that since the chemical structure of these accessory food substances is not definitely known, the term is probably a misnomer. This appears a splitting of hairs. Perhaps the term is not chemically exact, but neither is the use of the word ‘vaccine’ etymologically correct. Most vaccines have nothing to do with a cow. The term ‘vitamin’ is simply a convenient expression to use in place of the elaborate phrase ‘accessory food substance,’ and it will probably continue to be used because of its convenience. Vitamins are certainly necessary to life, and to that extent the term is etymologically correct and expresses a fact in one word which is lacking in the phrase ‘accessory food substance.’”

Beriberi, pellagra and scurvy are described by Vedder as “deficiency diseases.” He believes that dry beriberi and wet beriberi in man are caused by two distinct though perhaps chemically related vitamins.

As there are many conditions under which it is difficult for certain people and institutions to procure a rich and varied diet, Vedder emphasizes the following simple dietary rules for the prevention of deficiency diseases:

1. In any institution where bread is the staple article of diet, it should be made from whole wheat flour.
2. When rice is used in any quantity, the brown undermilled, or so-called hygienic rice, should be furnished.
3. Beans, peas or other legumes, known to prevent beriberi, should be served at least once a week. Canned beans or peas should not be used.

4. Some fresh vegetable or fruit should be issued at least once a week and preferably at least twice a week.

5. Barley, a known preventive of beriberi, should be used in all soups.

6. If cornmeal is the staple of diet, it should be yellow meal or water-ground meal, that is, made from the whole grain.

7. White potatoes and fresh meat, known preventives of beriberi and scurvy, should be served at least once a week, and preferably once daily.

8. The too exclusive use of canned goods must be carefully avoided.

Vedder is sure that the strict application of these rules will eradicate scurvy and beriberi, and believes that they would be equally efficacious in eradicating pellagra from the United States.

GASTRO-INTESTINAL TRACT.

DISEASES OF THE MOUTH.

Mercurial Stomatitis. The process by which this condition is produced and some suggestions as to its treatment are presented by Douglas W. Montgomery¹ of San Francisco.

He says that mercurial stomatitis is caused by the mercury administered, but in many of its manifestations is far from being directly due to it. The state of the mouth and very especially the sanitary condition of the teeth are of great importance in rendering the patient susceptible to mercury. The mere presence of the teeth is important, as shown by the infrequency of stomatitis in infancy and in toothless old age.

He points out that the well-known effect of mercury on the entire alimentary canal is an irritative one. The effect in the mouth is least marked in infants without teeth, or in adults whose teeth have been extracted, and most marked in those who have the most poorly kept teeth.

Mercury, therefore, when given to a man with a nor-

(1) Med. Record, Nov. 18, 1916.

mal mouth may, through its own physiologic action, cause highly disagreeable symptoms of a congestive nature, and when the oral cavity is ill-kept and irritable mercury is especially adapted to add seriously to his troubles.

The interaction in the mouth between putrefactive bacteria and mercury is given as worked out by Almkvist:

“When the proteid foods are pressed into the pockets about the teeth, or into the recesses of the mouth, they are attacked by the anaërobic putrefactive bacteria, principally the fusiform bacillus of Plaut-Vincent and the *Spirochaeta dentium*. Among other iniquities perpetrated, these bacteria form hydrogen disulphide gas.

When mercury is given, either by the mouth, by inunctions, or subcutaneously, it is principally taken up by the blood, and so circulates in the capillary loops of the papillae of the mucous membrane of the mouth. Here it comes in contact in the capillary wall with the above-mentioned sulphuretted hydrogen produced by the putrefactive bacteria, causing a precipitate in these capillary walls of the black sulphide of mercury. This black sulphide, HgS , although usually estimated as being insoluble, is only relatively so, as it exerts a detrimental action on the capillary loops, and interferes with the function of the vessels in transmitting nourishment, which in its turn, brings about degeneration and molecular death of the superimposed epithelium. This affected epithelium constitutes, therefore, additional dead proteid matter, furnishing still more nutriment to the anaërobic putrefactive bacteria, and so on progressively leading to erosions and to ulcerations of greater or less extent and depth, abscess formation, periostitis, necrosis, for instance of the lower jaw, and even the death of the patient.

Many factors are involved in the etiology of stomatitis besides the direct action of the mercury itself. There is the previous state of the mouth, the stomach, and the alimentary canal, the presence of the anaërobic bacteria and the susceptibility of the patient to their deleterious action, and the sensitiveness of the individual patient to the drug mercury itself. Intricate as the disease,

hydrargyris, is, there is a distinct advantage in appreciating these different etiologic factors and in knowing where trouble is likely to break out, as giving a greater objectivity and intelligence to therapeutic measures. The other danger of being so cautious as to render the treatment of syphilis ineffective out of fear for the remedy is also to be remembered.

In the treatment of the condition Montgomery recommends the following preparations:

R Sol. perhydroli, 5.00.

Aq. ad., 200.00.

M. Sig.: A teaspoonful in a half or a full glass of water as a mouth wash, several times a day.

As peroxide of hydrogen is one-tenth the strength of perhydrol an equivalent prescription would be:

R Peroxide of hydrogen, 50.00.

Aq. ad., 200.00.

M. Sig.: A teaspoonful in a half or a full glass of water.

Perhydrol is a 30 per cent. solution of peroxide of hydrogen free from acid.

R Peroxide of hydrogen.

Argent. nitric. (20 per cent. sol.) aa, 10.00.

M. Sig.: Apply with a cotton swab.

Both chlorate of potassium and peroxide of hydrogen, the two remedies found so valuable in mercurial stomatitis, give off their oxygen very readily, and it may be presumed that it is to this circumstance that they, in a great measure, owe their effect in interfering with the activity of the anaërobic bacteria.

A 10 per cent. solution of chromic acid is said to be a good application for erosions. The following preparation is recommended by the author when the gums are in good order:

R Tr. rhataniae.

Tr. gallarum, aa 15.00.

M. Sig.: Fifteen to twenty drops in a half glass of water as a mouth wash.

If inunctions have been used the patient should have a good scrubbing with soap and water to remove as much as possible of the mercury from the skin. Besides this,

there should be free catharsis, as it has been found that mercury is eliminated most by way of the bowel. The author advises against the use of atropine and belladonna since they are liable to decrease not only the flow of saliva but also of other secretions that are of importance for proper elimination of waste from the body.

Treatment of Stomatitis and Vincent's Angina by Methylene Blue and Silver Nitrate. In their treatment of about twenty cases, M. Favre and H. Dreyfouss² report remarkable success from the following technique: The membrane covering the ulcers is thoroughly removed by means of a cotton applicator. The surface is then gone over with 10 per cent. silver nitrate solution several times. After this, a 1 per cent. solution of methylene blue is applied by painting the surface carefully. The same procedure is repeated each day. After two or three treatments healthy granulation tissue makes its appearance and then the silver nitrate is reduced to 3 per cent., and the treatments continued until complete cure.

Treatment of Oral Sepsis. In a note of warning with regard to the treatment of oral sepsis, J. M. Anders,³ of Philadelphia, quotes the opinion of a number of leading dentists, who are inclined to think that many physicians of the present day are directing dentists to extract teeth when this is entirely unnecessary. The diagnosis of ulcers about the roots of teeth by means of x-rays, which, it is said, are frequently faulty, and the pulling of large numbers of teeth on the suspicion that they may have some bearing on a condition diagnosed as due to a sepsis from focal infection in some parts, is considered without justification.

Anders states that, in secondary systemic infections, our present-day views of treatment demand the removal of the focus or foci on which they depend. A cure, or permanent improvement even, is not possible by pursuing any other course, but the physician should be thrice certain that the teeth are septic and not amenable to skillful dental management before he advises their extraction. Moreover, it is to be recollected that in a certain percentage of such instances there are multiple

(2) Presse méd., Nov. 2, 1916.

(3) New York Med. Jour., March 10, 1917.

foci of infection, and while this is often true of the teeth it not infrequently happens that additional and larger ones harboring more virulent microorganisms are to be found elsewhere, *e. g.*, in the tonsils and sinuses, and unless these be removed, failure to relieve the systemic infection is an inevitable result.

The fact that chronic septic foci are exceedingly difficult to diagnose in the majority of cases needs to be emphasized. A single examination, however carefully made, fails to clear the diagnosis in many cases at least. Peri-apical infection and abscess offer the greatest difficulty in this respect. Here, even an *x*-ray examination may fail to render reliable aid. In these cases, the dental specialist investigates the condition of the pulp canal from apex to the extreme base. Should this exploration still leave the case in doubt, he should take a further step and aspirate the peri-apical space under strict antiseptic precautions and culture the withdrawn material. If now one of the salivarius group of streptococci, *e. g.*, the *S. viridans*, *S. hemolyticus*, or *S. mucosus*, be discovered, then the diagnosis is correct.

Anders insists that judgment of both physician and dentist should prevail as to whether or not teeth should be extracted in cases in which they are suspected of being the focus of a more general infection.

Tuberculosis of the Tongue. This case is reported by W. C. White and C. H. Marcy,⁴ of Pittsburg. The patient was a man aged 30, with ulcer of the tongue, the chief symptoms of which were soreness and swelling. The pain was so severe when food was taken that the man could not eat, and he had lost twenty pounds in five months.

His home physician treated the ulcer locally with silver nitrate and iodine for five months. Only by the use of cocaine locally was the man able to take nourishment. He lost ten pounds in weight in two months in the hospital, and the ulcer continued to increase in size. The surgeon's advice was to excise the tongue wide of the lesion. The authors suggested that a trial be given to injection of tuberculin into the base of the lingual ulcer. This was done. At the end of twenty-four

(4) Bull. Johns Hopkins Hosp., May, 1917.

hours the tongue was swollen, red and a little more painful. At the end of forty-eight hours it was still slightly swollen, but not sore, and the increased redness was fading. After this the ulcer commenced to diminish in size, until at the end of one week it was not more than half the size and the patient was able to eat without pain. Two weeks later a second dose was given in the same way. One week later a reduction occurred of approximately 50 per cent. in the size of the ulcer. A third injection was given two weeks after the second. Twelve days later the ulcer had almost completely healed and the man was again rapidly improving in weight and health. A fourth dose of tuberculin was given when the ulcer was quite healed, and only a small fissure left to mark its former site.

Ulcer of the Esophagus Causing Fatal Hemorrhage. This case is reported by J. B. Christopherson.⁵ The patient was a man of 36, and sought medical attention because he thought that he had something in his throat. As he had first noticed a feeling of discomfort after dinner on the previous day, when he had eaten fish, he thought that a fish-bone might have lodged in his throat.

There being no clinical evidence of fish-bone or foreign body, he was put to bed and given expectant treatment. His symptoms were as follows: He felt as if there was "something in the chest"; he felt it when he swallowed, more especially when he swallowed "nothing" and also when he drew a deep breath. He located this sensation, which was more discomfort than pain, inside the chest behind the sternum, at a place which would correspond to the level where the ulcer was eventually found. He also had some pain behind, between the shoulder-blades. There was nothing to be seen in the throat, no physical signs of anything amiss in the chest, and, in fact, the only symptoms indicating that there was anything wrong were a rise of temperature to 100° F., a coated tongue, and discomfort, sometimes amounting to a little pain, on swallowing or drawing a deep breath. Seven days later he had a large hemorrhage, and one day after this the fatal hemor-

(5) *Lancet*, March 10, 1917.

rhage occurred. At the necropsy it was found that the hemorrhage came from an esophageal ulcer which had become adherent to the descending part of the arch of the aorta, in the neighborhood of the bifurcation of the trachea and which had penetrated the arterial wall. There were two other ulcers in the esophagus, both situated at the cardiac end just within the esophagus, one of which had healed with a cicatrix, and the other, a larger oval one, in the process of healing.

DISEASES OF THE STOMACH.

Clinical Study of the Secretion on the Proximal and Distal Sides of the Pylorus. This article by A. S. Robinson¹ is based on the study of 125 patients with various gastro-intestinal disturbances. Secretions were obtained from the fasting stomach in all cases and many times both the secretory and motor functions of the stomach were determined.

The average gastric secretion of the fasting stomach was found to be a clear opalescent fluid. About 10 c.c. could be aspirated every ten minutes. A small amount of mucus was invariably present. In the same individual the acidity of the fasting stomach was found to be about one-half that of the acidity after an Ewald test meal. Microscopic examination showed small shreds of mucus. A few white blood cells, usually clumped in mucus, were found, and some degenerated squamous epithelium and bacteria of varying types.

The normal duodenal secretion is of a clear amber color. About 15 c.c. can be obtained every ten minutes. There is no free hydrochloric acid present, the total acidity being about 5 per cent. lower than that of the gastric secretions. It remains of an amber color for several days, gradually changing to green as the bilirubin becomes oxidized to biliverdin. Microscopic examination shows fewer white blood cells, epithelium and bacteria. A large diplococcus was the commonest type seen. When free hydrochloric acid is present, the bile pigments are precipitated. Instead of a clear amber, the fluid is of

(1) Archiv. Int. Med., February, 1917.

a cloudy yellow color, and a sediment settles on standing. It becomes green very rapidly, depending on the amount of free hydrochloric acid. Microscopically, a fine yellow sediment is seen, which resembles amorphous urates.

On neutralizing the free hydrochloric acid with sodium hydroxide, the fluid becomes of a clear amber color.

In this group of patients, 40 per cent. of the disorders were classified as gastric neuroses; these were subdivided into gastric neurosis secondary to infection, as tuberculosis, influenza, syphilis and pelvic inflammatory condition; second, gastric neurosis associated with chronic constipation; third, gastric neurosis secondary to some mental or physical strain.

In these cases nothing pathologic could be found to account for distress. Diagnosis of a pathologic condition can not be made from subjective symptoms.

Gastric neurosis is most commonly secondary to an infection, as tuberculosis, syphilis, influenza, constipation and mental and physical strain.

The secretions on the proximal and distal sides of the pylorus and the gastric acidity curves show nothing constant or typical of this position.

In eighteen of Robinson's patients the definite positive diagnosis of gastric ulcer was made. The duodenal tube was passed through the pylorus in only two of these cases. Twelve were given modifications of the Sippy routine as indicated in the following chart:

Days.	Milk and cream, ounces of each, 6 a.m. to 8 p.m.	Soft eggs, a.m. p.m.	Cereal and sugar, oz.	Cream soups, oz.	Jel- lies, oz.	Stewed fruit.	Toast.
1	$\frac{1}{2}$ per hour
2	1 per hour
3	$1\frac{1}{2}$ per hour
4	$1\frac{1}{2}$ per hour	1	1
5	$1\frac{1}{2}$ per hour	2	2
6	$1\frac{1}{2}$ per hour	2	2	3 noon
7	$1\frac{1}{2}$ per hour	2	2	3 twice a day
7 to 14	$1\frac{1}{2}$ every 2 hrs.	2	2	3 twice a day	3
14 to 21	$1\frac{1}{2}$ every 2 hrs.	2	2	3 twice a day	3	3	2
21 to 28	$1\frac{1}{2}$ every 2 hrs.	2	2	3 twice a day	3	3	3
							Twice a day

Before discharging the patients, they were given a liberal diet, with no alkalies. A test-meal was then obtained. If they had a return of the gastric symptoms, or if the gastric analysis showed hyperacidity, they were advised to continue taking alkalies and a suitable diet was suggested.

The treatment used in conjunction with the diet, outlined as the modified Sippy diet, is called a modified B. W. Sippy treatment for gastric ulcer and is as follows:

Absolute rest in bed for three weeks, with 1 dram of bismuth subcarbonate in 3 ounces of water each morning before feedings are begun.

Midway between the feedings the two following are given alternately:

Ten grains each of heavy calcined magnesia and sodium bicarbonate in $\frac{1}{2}$ ounce of water.

Ten grains each of bismuth subcarbonate and sodium bicarbonate in $\frac{1}{2}$ ounce of water.

Next a comparison was made between the acidity curve of the fasting stomach and that after an Ewald meal in various pathologic conditions. In making this comparison no uniformity was found, no curve was demonstrated as typical of a gastric ulcer or of the duodenal ulcer. In the latter condition, however, the acidity was greater and the stomach emptied itself sooner than in other conditions. No curve was found which was thought to represent the normal acidity, nor was a curve found which was considered typical of a certain pathologic condition. There was no relation between the acidity curve of the fasting secretions and those obtained after a test-meal in the same individual. The average curve in carcinoma and pernicious anemia has a tendency to descend, in other conditions to ascend. The highest percentage was in duodenal ulcers.

Further, concerning duodenal ulcers the author says that the gastric secretions of the fasting stomach showed, as a rule, a greater acidity than was found in other conditions. The color was not abnormal. The duodenal secretions, in addition to the presence of blood, contained an increased amount of exfoliated epithelium and white blood cells.

From an investigation of the secretions in the patients with cholelithiasis it is said that duodenal secretions found in four such patients having more or less typical symptoms of gall-stones, contained a heavy sediment which was different from that in other cases, was heavier and of an orange-yellow color. The duodenal secretions were cloudy, microscopically the individual particles of detritus were larger and more highly colored than those precipitated by acid. It stained very poorly with methylene blue.

On finding an orange-yellow, coarse detritus in the duodenal secretions, together with a history of colicky pains, or jaundice, a positive diagnosis of numerous gall-stones can be made. No abnormal findings were present in the duodenal secretions in cases of cholelithiasis in which only one stone was present.

As a summary of the findings in cases of cholecystitis, the following points are mentioned:

The normal alkaline duodenal secretion has a clear, amber color.

The presence of free hydrochloric acid produces a cloudy yellow duodenal secretion, which becomes clear when neutralized.

An alkaline duodenal secretion that is cloudy is suggestive of an inflammatory condition in the duodenum or biliary tract. The cloud is due to the presence of bacteria and pus. It does not clear on the addition of sodium hydroxide. Epithelial and white blood cells, which are stained yellow by the bile pigment, do not necessarily come from the biliary tract. They may be stained while in the duodenum by the precipitation of bile pigment by the free hydrochloric acid in the stomach. Colon bacilli are occasionally present in the duodenum. The level in the duodenum at which they appear varies.

A number of patients with pernicious anemia were investigated. Considering the theory that this disease is caused by hemolytic agents and that this agent is dependent on a disturbance of the gastro-intestinal tract, the author attempted to find out if there were present in the gastric and duodenal secretions any substance which had a greater hemolytic action than in normal secretions.

The hemolytic power of the secretions on the proximal and distal sides of the pylorus was determined on six patients, who were not anemic. Another series of six tests on six patients suffering with pernicious anemia was done. The results of this series, without a single exception, showed that the gastric and duodenal secretions from cases of pernicious anemia caused no more hemolysis than do normal secretions.

Fractional Gastric Analysis. An account of fractional determination of gastric secretions in sixty-five patients is presented by Ernest C. Fishbaugh.²

After a brief review of the literature on this subject, he says that the technique followed in his study has been,

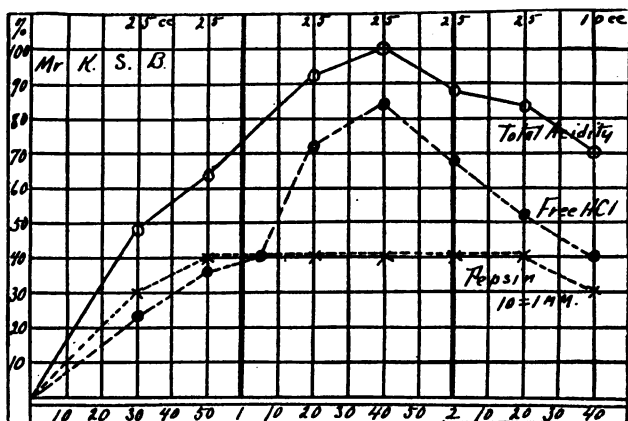


Fig. 9.

in the main, that of Rehfuess, with variations in details only. Forty grams of water-crackers with 10 ounces of water, about 2 ounces of which were reserved to be swallowed with the tube, were given as a test-breakfast. Usually about ten minutes were required for the ingestion of the crackers and water. Immediately the tube was swallowed with the remainder of the water. The excess of saliva which formed rapidly during the first few minutes was expectorated. If the saliva was swal-

(2) Jour. Amer. Med. Ass'n., Oct. 28, 1916.

lowed it interfered materially with the ease of the aspirations. After the first few minutes the patient suffered no inconvenience with the tube in his mouth. The patient was placed at ease, either sitting or lying down, and urged to read or otherwise divert his attention. At twenty-minute intervals, from 15 to 25 c.c. of the stomach contents were withdrawn until the stomach was empty. The aspirations were made by gentle suction.

The author says that in reviewing the fractional studies of sixty-five gastric cases, the value of the interval method of stomach analysis becomes evident. The

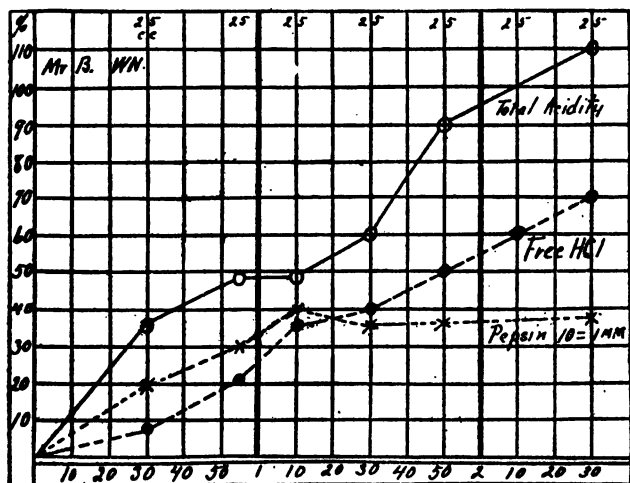


Fig. 10.

ordinary one-hour examination evidences a single moment in an ever-changing cycle of stomach activity. The one-hour examination not only affords insufficient information but also gives data which frequently are misleading or entirely incorrect. Irrespective of symptomatology and physical diagnosis, it was noted that aside from emphasizing the value of the method, the curves of stomach secretions fell into three general classes:

Stomach secretions whose curves fall toward the end of gastric digestion.

Stomach secretions whose curves rise to the end of gastric digestion.

Stomach secretions absent or delayed.

In the first group there were twenty-six; in the second, twenty-four, and in the third, fifteen.

The third group is further subdivided into three others:

Absence of acid and enzymes, of which there were two instances.

Absence of acid, with enzymes present; the most common of which were represented in this series by ten cases.

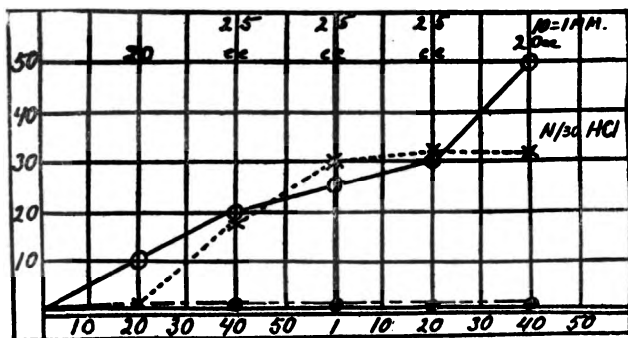


Fig. 11.

Enzymes and acid appearing late in the cycle of digestion, of which there were three examples.

The accompanying charts (Figs. 9-11) are self-explanatory, and illustrate the points in the different types of secretion described here.

Among his conclusions the author states that the one-hour stomach examination affords insufficient and often misleading information concerning the acidity and enzyme secretion. It gives no evidence of the secretory curve. The fractional method of stomach examination follows the entire cycle of digestion, and supplies reliable information concerning the type of secretory curve, the degree of acidity, the ferment content and accurate estimation of the emptying time.

Clinical Importance of Determination of Pepsin in the Stomach Content. In this article, T. Hernando and T. Alday³ state that while they found the Mett technique the most exact, and the Fuld-Levison the simplest, for all practical purposes the Boas method is sufficiently reliable.

They report that in ten cases of anachlorhydria pepsin was always present in their tests although in proportions much less than normal. Each case should be determined separately in watching the progress of a stomach affection.

In ten cases of non-cancerous hypochlorhydria, the proportion of pepsin was unusually low in some but normal in others.

In twenty-two cases of gastric cancer, no pepsin could be detected in three cases by the Mett technique; in sixteen only small amounts; in one it was normal and in two above normal.

With the Fuld method in twenty-nine cases no pepsin could be found in six cases, very little in twenty-one, and the findings were normal or above normal in one case each.

In eighteen cases there was a deficit of hydrochloric acid and in six it was present only in moderate amounts.

In thirty cases of hyperchlorhydria (Mett) the pepsin content was normal or subnormal in four cases each and in twenty-two above normal. With the Fuld technique, in thirty-five cases, it was normal in twelve and above the normal range in the others.

In all the thirty-seven gastric or duodenal ulcer cases, and in thirty-four of thirty-five (Mett) cases and in forty-eight of fifty (Fuld) cases of cicatricial stenosis of the pylorus, the pepsin was much above normal. Hence, the authors say, this finding should suggest the possibility of an ulcer. It is possible that in some of the hyperacid cases with high pepsin content there may have been some undetected ulceration. Certain measures known to influence ulcer favorably may owe their efficacy to their action on the pepsin, rather than on the acidity, to which it is generally attributed. This applies particularly to sodium chloride which

(3) *Siglo med. Madrid*, March 3, 1917.

seems to have an inhibiting influence on pepsin. Inert powders, to absorb it, have a similar inhibiting action. Their experience indicates that the pepsin content may aid in the prognosis with hyperchlorhydria, the outlook being better when the pepsin content is low. The authors warn that pepsin should never be given alone or with an alkali. It requires an acid medium to be effectual. In chronic gastritis of the catarrhal type, tending to atrophy, they found the pepsin content low as a rule.

Intragastric Temperature. This is a report of a new method for determining the intragastric temperature in man, with some observations on its variations after ingestion of hot and cold liquids and during digestion by Alfred Stengel and Arthur H. Hopkins,⁴ of Philadelphia.

The apparatus employed in these studies consisted of a thermocouple of copper and constantin wires, one pair of ends being placed in a thermos bottle 0 degrees C. and the other pair being soldered together and run through an Einhorn duodenal tube, at the end of which they were made secure within the small perforated metal bulb. The thermocouple was then joined to a mirror galvanometer and a potentiometer, the readings being taken in microvolts. This instrument was so calibrated that 40 microvolts corresponded to 1 degree C., with slight variations at the ends of the scale. Readings could thus be taken within one-fortieth of a degree C. (Fig. 12).

The accompanying table shows the comparison of temperature in the fundus and the pyloric portion of the stomach after ingestion of cold liquid.

Case.	Temperature before water taken.			Drop in temperature.		Time to return to normal.
	Fundus.	Pylorus.	Ice-water.	Fundus.	Pylorus.	
1.	38.0° C.	38.0° C.	120 c.c.	14.2° C.	8.9° C.	20
2.	37.9° C.	37.9° C.	120 c.c.	6.4° C.	5.1° C.	19
3.	37.9° C.	37.0° C.	120 c.c.	8.1° C.	1.2° C.	30
4.	36.9° C.	36.9° C.	120 c.c.	5.2° C.	1.0° C.	31
5.	36.9° C.	36.9° C.	120 c.c.	12.8° C.	8.7° C.	24

The observations recorded in this table show the prolonged time required for the return to normal tempera-

(4) Amer. Jour. Med. Sci., January, 1917.

ture, considering the small amount of liquid taken, also the marked drop in temperature at the fundus, and the striking difference in fundic and pyloric regions. The great difference in temperature of fundus and pylorus after the introduction of cold drinks or ice cream, as well as the length of time required for the stomach to resume normal temperature, are of special interest in that they confirm from a different standpoint the comparatively recent researches of Grutzner, Cannon and others.

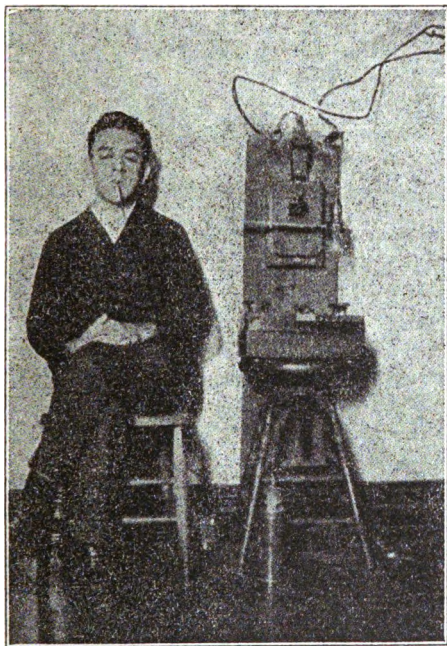


Fig. 12. Photographs illustrating the authors' instrument used in estimating intragastric temperature: A, Einhorn duodenal tube containing the thermocouple; B, mirror galvanometer; C, Potentiometer.

Large meals with hot and moderately cold food mixed showed slight transient fluctuations with the bulb alternating between fundus and pylorus; but when at the end of the meal ice-cream was taken there was a drop

of 7.9 degrees C. at the fundus and 3.3 degrees C. at the pylorus, and forty-five minutes were required for the resumption of normal temperature, which occurred at both areas at nearly the same time. When hot coffee was taken after the ice-cream an immediate return to normal temperature was experienced.

Observations were made on the temperature of the stomach during digestion eliminating the factor of variations of temperature of food. The bulb having been introduced into the fundus, the patient was given 360 c.c. of milk and two slices of bread heated to body temperature. Oral and rectal controls were taken at frequent intervals. No changes were demonstrable in the intra-gastric temperature during a period of over one hour in any of the cases observed.

In the study of the effects of local applications ice-bags were applied over the gastric area and were found to produce an average drop of from 0.9 degree to 1 degree C. in the course of forty-five minutes. The effect of hot-water bottles applied in the same position was very slight—in fact almost a negligible factor during three-quarters of an hour.

In this article the authors detail only the results of their observations without making any practical deductions at this time. They say that it is obvious that hot and cold foods taken alternately may influence the functions of digestion favorably or otherwise.

The Significance of Appetite and Secretion of Gastric Juice in Practical Medicine. In this article A. J. Carlson,⁵ Professor of Physiology at the University of Chicago, refers to the classical work on physiology of the stomach and stomach secretions, by Pavlow. This noted Russian physiologist carried out work which led to the general conclusion that appetite is of importance in digestion and nutrition essentially because it leads to an abundant secretion of gastric juice, the so-called appetite or psychic gastric juice. Pavlow and his co-workers showed in dogs that seeing, smelling and particularly the tasting of palatable food resulted on the part of the hungry in secretion of gastric juice of the highest acidity and pepsin concentration. In fact, the physiologist states that

(⁵) Interstate Med. Jour.

no other stimuli to gastric secretions can compare, so far as quantity and quality of the juice is concerned, with the desire for food.

Pavlov also stated that in the absence of food in the stomach and in the absence of psychic factors of appetite, that is, seeing, tasting or smelling food, not a drop of gastric juice flows from the little stomach pouch of the dog used in his experimental work. This view, says Carlson, is erroneous. So far as the latter's experience goes, and his experience includes observations on many hundreds of dogs, and from 75 to 100 normal persons, secretion of gastric juice by the empty stomach in the total absence of food or appetite factors is almost invariably the rule. This secretion rate in normal persons varies from a few cubic centimeters to as much as 125 c.c. an hour. The higher the rate of this continuous secretion the nearer does the product approach in composition the full acidity and pepsin concentration of pure appetite gastric juice. The cause of the continuous secretion remains unknown. Carlson thinks that the secretory rate in the empty stomach is as high as 125 c.c. an hour. It is apt to be regarded by the physician as a hypersecretion, in other words, a pathologic phenomenon. But in the persons under Carlson's observations there was absolutely no evidence of gastro-intestinal disorders or other pathologic conditions in any part of the body.

Carlson has for a number of years had the opportunity of studying appetite gastric juice and the secretion of gastric juice in a normal person with a permanent gastric fistula and a complete occlusion of the esophagus of over twenty years' standing. In this man he found that the average rate of secretion of appetite gastric juice was 3.5 c.c. a minute. The maximum rate of secretion that has been observed during mastication of a meal was 11 c.c. a minute; the lowest, 1.5 c.c. a minute. Chewing the food without appetite causes no secretion of gastric juice whatever. A man, seeing, smelling or thinking of food when hungry, has a very slight influence on the continuous secretion of gastric juice. In this respect, man appears to differ from dogs, as studied by Pavlov. In man, the all-important factor for the appe-

tite secretion is the tasting or the chewing of the palatable food. The secretion starts practically without any latent period as soon as the person starts to chew, and it begins to slow up practically at once when the mouth

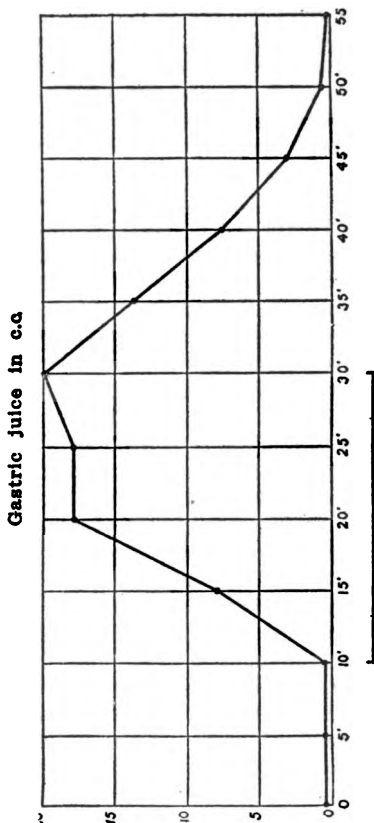


Fig. 13. Typical curve of secretion of gastric juice of Mr. V. on mastication of palatable food for twenty minutes. The gastric juice was collected at five-minute intervals. The rise in the secretion rate during the last five minutes of mastication is due to chewing the dessert (fruit).

is free from food, so that in from 15 to 20 minutes after chewing the food the appetite secretion factor is at an end. A typical curve of appetite secretion of gastric juice in man is reproduced in the accompanying chart (Fig. 13). This appetite gastric juice in normal persons

is of a very constant composition. The total acidity is practically 0.5 per cent. or the same as in a normal dog.

The author points out that in this connection the acidity of this pure gastric juice from the stomach of normal persons is equal to the highest degree of acidity of the gastric juice so far recorded in the literature in cases of so-called clinical hyperacidity.

Concerning the significance of appetite and appetite gastric juice for digestion and nutrition in man, he says that appetite depends not only on memory processes of past experience with palatable food as positive phases, and the memory process of removal of hunger pangs by feeding, but the presence of this memory process in consciousness depends on certain conditions of the alimentary tract. When the stream of afferent impulses from the alimentary tract and possibly other visceral organs becomes altered in quantity or quality from the normal, these impulses suppress or render impossible the existence of appetite. Hence it would appear that existence of appetite is an indication of a proper condition of the alimentary tract to handle the food in the way of motility and secretion, and that this is the chief biologic significance of appetite. The production of appetite gastric juice is of secondary importance and of practical significance only in cases of extreme impairment of gastric secretion.

It seems clear, says Carlson, that a continuous secretion of gastric juice in the stomach of normal man and animals, in the total absence of food in the stomach and of psychic stimulation, is sufficient to initiate gastric digestion, and, therefore, to ensure sufficiency of gastric secretion, provided the condition of the gastric glands and of gastric and intestinal motility are normal. The appetite secretion of gastric juice is simply an accessory factor of safety. In the normal stomach it does not appear to be needed at all.

These new aspects of appetite and appetite gastric secretion minimize the importance of the various therapeutic measures that are supposed to induce or augment the appetite gastric juice. It emphasizes at the same time the importance of more complete analysis of appe-

tite and establishment of practical measures of control of appetite itself as a real problem.

[These views of Carlson are safe and sane, and will undoubtedly stand the test of time. They clearly demonstrate the value of presenting to the sick dainty and tempting dishes in an appetizing manner and suitable environment. Good nursing, good dietetics, and coaxing methods of serving have long been regarded as essential in the sick-room. Now we know that they rest upon a sound basis of scientific observation and reasoning. The old concept that hyperacidity stimulates appetite must give place to the new one that appetite stimulates hyperacidity.—GEN. ED.]

Correlation of Clinical and Roentgen data in the Diagnosis of Gastro-Intestinal Lesions. J. A. Matlack,⁶ of Galesburg, Ill., emphasizes the great importance of roentgenologic and clinical findings depending upon one another, in arriving at a final diagnosis of lesions of the gastro-intestinal tract. There are *x-ray* workers who are extreme enough to maintain that their diagnoses are more nearly correct than those of the clinician and *vice versa*. The author discusses the factors of importance to the clinician in obtaining history, doing laboratory work, and physical findings to make the diagnosis, especially of the esophagus and stomach and the duodenum. The value of *x-ray* findings in such conditions as reflex disturbance originating in other organs, such as the gall-bladder and appendix, and in certain cases of neurasthenia in which the patients constantly complain of the stomach or of intestinal trouble, and in neurasthenic patients who have come to believe that some particular trouble is located in the stomach or intestines, is especially emphasized.

From the *x-ray* point of view, Matlack says that, strictly speaking, the roentgenologist should confine his work to the observation of radiographic shadows and to the recording of such shadows as to their size, shape, density, and location. In rendering visible a hollow viscus by means of opaque media, a strict *x-ray* interpretation would lie merely in the observation of the shadow cast by such media—whether the viscus receives

(6) Interstate Med. Jour., January, 1917.

it in a normal manner and with normally developing contour, or whether a distortion, obstruction, filling defect or other abnormality is demonstrable. If the roentgenologist undertakes to interpret these shadows as pathologic entities, he will frequently fall into error, unless he gets clinical information either directly or indirectly from the patient or from the clinical consultant. For instance, the shadow of an irregular filling defect in the mid-portion of the esophagus usually means carcinoma, but the finding is conclusive only in case the patient shows the clinical picture of malignant disease. A similar shadow in a patient who gives a history of swallowing a caustic solution probably means a benign stricture.

An obstruction low in the esophagus, giving a smooth shadow, suggests cardiospasm, and one of irregular outline suggests carcinoma, but it is quite possible for a carcinoma to have a smooth shadow, and a cardiospasm may be complicated by the presence of solid food particles and thus cast a shadow of irregular outline.

A definite deformity of the first portion of the duodenum in the great majority of cases signifies duodenal ulcer, but in the occasional case it may be due to adhesions or other extraneous causes. Consideration of the clinical aspects may be needed to clarify the situation. Likewise, a definite filling defect in the stomach or colon usually means carcinoma, but in a small percentage of cases the condition is due to syphilis, extraneous pressure, spasm, or inflammatory conditions. Here, also, clinical information is essential. In those and similar cases it is impossible to formulate any rule of shadow interpretation which will hold good without many qualifying exceptions, and it is therefore necessary for the roentgenologist to take cognizance of clinical factors if he elects to report lesions instead of confining himself to the description of shadows.

The conclusion is this, says Matlack: The *x-ray* interpretation of gastro-intestinal lesions has been developed on a sure foundation and can not be ignored by the progressive clinician; and also, without the help of the clinician the roentgenologist is more or less at sea in the interpretation of his findings. The correct diagnosis will be arrived at either by the combination of clinician and

roentgenologist in the same individual, or else by close and friendly coöperation between the individuals, each with a proper respect for the work of the other.

Diagnosis of Stomach Affections Without the Stomach Tube. R. Landerer⁵ quotes Boas' list of sixteen conditions in which the use of the stomach tube is contra-indicated, but does not agree with him that gastric neuroses are always a contra-indication. It may be important to convince the patient by the stomach-tube findings that he has no organic gastric trouble. Neurasthenia may be the primary trouble, but the general practitioner can demonstrate this only by exclusion. Roentgen examination reveals motor disturbances, and there are no contra-indications for this. Aside from these methods of examination, much can be learned from inspection of vomited material. If the reaction is alkaline or neutral, this may be due to admixture of saliva, etc. But if it is acid, and the acid proves to be hydrochloric acid, then it must have come from the stomach. If present in excessive amounts, hyperacidity is beyond question. The presence of lactic acid is not so conclusive in vomitus as in the siphoned-out stomach content. Determination in vomitus of the digestion of starch is of little use as the saliva may have coöperated; admixture of blood is also unreliable. If rennin and pepsin are found, the findings are conclusive, but if they are not found, it is impossible to say whether they might not have been inactivated or destroyed by fermentation.

All the findings in vomited material are of merely presumptive import; similar findings in fresh siphoned-out stomach content are conclusive. When it is impossible to use the stomach tube, the patient must be put on a test diet and the stools examined. This is tedious, as the individual has to stay in bed for three days and receives only the unappetizing test diet. As the stomach gets upset ten times at least to the pancreas' once, the finding of undigested muscle fibers and of fat points usually to the stomach. Occult blood should always be sought if there is the least suspicion of ulcer or cancer. In case of dubious findings, Landerer asks: "Which is worse for the patient, to take a course of treatment for

(5) Med. Klinik, Oct. 15, 1916.

a suspected but really non-existent ulcer or to have ulceration overlooked?" It is important further to estimate the effect of treatment of an ulcer by examining the stools for blood. No patient should be discharged as cured until findings have been negative several times.

When a patient has good appetite and good gastric digestion but a tendency to diarrhea, this suggests a deficit of hydrochloric acid in the stomach. By giving a little hydrochloric acid in water, after a meal, it usually passes at once into the small intestine, but from there it may excite the normal reflex closure of the pylorus, and thus enable the food to be kept longer in the stomach and be better digested than would be the case without the therapeutic acid. This may explain the improvement under fat in some cases of achylia; the fat checks motor functioning and the food is kept longer in the stomach. Pain in the stomach that subsides when something is eaten is regarded as a sign of hyperacidity, but this is more certain when the pain can be checked by giving an alkali.

Separation of Stomach Diseases Into Diagnostic Groups. The separation of a large number of patients suffering with stomach disease into diagnostic groups has been made by William Fitch Cheney,⁶ of the Leland Stanford, Jr., University School of Medicine. From a total of 2,116 records of patients during the last five years, this author has found 297 classified as complaining of some gastric disturbance. Dividing this number of patients suffering with diseases of the stomach into various groups, the first is that of gastric cancer; twenty-eight cases were recorded in this group, and in all the diagnosis was verified by operation or by necropsy. In mentioning the various items in regard to cancer, Cheney says that those originating in the cardiac end of the stomach very early give rise to dysphagia, with regurgitation of food soon after it is eaten, but may show free hydrochloric acid, if the stomach contents can be obtained. No tumor may ever be palpable at any time. Cancer of the lesser curvature is marked by loss of appetite, bloating, pain after eating, loss of weight, strength and color; it may become very large before it

(6) Jour. Amer. Med. Ass'n., May 19, 1917.

is palpable or before hydrochloric acid disappears from the stomach contents.

Points of importance in diagnosis are as follows: Two of the patients were under 40 years of age, one 37 and one 35. In twenty-three of the cases the duration of the symptoms was set down as one year or less, some only a few months, for short duration of symptoms with rapid progress is characteristic of gastric cancer.

In seventeen of these patients chemical analysis showed complete absence of free hydrochloric acid, as was expected. Tumor was found by palpation of the abdomen in twenty of the cases, but was not palpable in eight. In every one of the cases in which no tumor could be felt, its presence and location were distinctly shown on the roentgenographic plate.

The second group contains patients who suffered from gastric and duodenal ulcers. The propriety of including duodenal ulcer in this group is said to be now scarcely questioned. It has been proved that in etiology and pathology, gastric and duodenal ulcers are identical. Ninety-two patients were assigned to this group; of these, fifty-five were considered to be gastric, thirty-seven duodenal. Twenty-three of these patients came to operation, at which nine ulcers proved to be gastric and fourteen duodenal. Several ulcers diagnosed as gastric were found at operation to be duodenal, and one diagnosed as duodenal proved to be gastric.

Points of importance in the history of these patients were the chronicity; the time of symptoms as decided by the patient varied from two or three to twenty years; a more common period was from five to ten years.

Periodicity was of marked frequency; there were times of weeks or months during which the symptoms persisted, followed by days, weeks or months of remission or complete intermission. The most constant complaint was that of pain; so essential is this that without it the diagnosis of ulcer is always a dubious one. The site of the pain and time of occurrence are variable in different patients. Almost universally the story is that pain is relieved by taking food and does not recur for an hour or more afterward. Accompanying symptoms were belching, waterbrash, heartburn, and nausea.

Gross hemorrhage was the unusual symptom in this series. Physical examination of the abdomen does not afford much direct evidence in the chronic gastric or duodenal ulcer. Tenderness and rigidity were noted frequently over the gastric area, sometimes localized to one sensitive spot, but this occurs with gastric diseases other than ulcer, and on the other hand is not always found even when ulcer exists.

Cheney thinks that it is a mistake to assign too much importance to the element of hyperacidity in diagnosis. Gastric ulcer may be present even with normal or sub-normal acidity. Of these patients the total acidity was over 100 in three; between 90 and 100 in eight; between 80 and 90 in sixteen; between 70 and 80 in nineteen; between 60 and 70 in twenty-eight. If the range of normal total acidity is assumed to be from 40 to 60, as is the usual rule, there were thus seventy-four of these cases which showed a hyperacidity, but there were seven between 50 and 60, and six between 40 and 50.

Occult blood in stomach contents is too common a finding after extraction of test meals to be of any value whatever as a sign of disease; and unless occult blood in feces is found after most careful preparation of the patient by days of meat-free diet, unless all other possible sources of bleeding from the gums to the anus have been eliminated, and unless it is persistently found, this sign has but little value in the diagnosis of gastric or duodenal ulcer.

[To the editor this statement seems too sweeping. The finding of occult blood three days in succession in the feces of a patient on a milk and egg diet for five days, two days preceding the tests and three days during the tests, is good evidence of the presence of blood. Furthermore, other possible sources of bleeding from gums to anus can, as a rule, be readily discovered.—GEN. ED.]

The evidence furnished by a fluoroscopic examination and roentgenographic plates is undoubtedly the greatest advance made in the knowledge of gastric and duodenal ulcer in the past decade. Facts as to the size, position and shape of the stomach, its peristaltic activity, its emptying time, its contour and its possible defects are all of immense value in proving the significance of symptoms

and secretory findings; while the contour and outlines of the duodenum, as shown by roentgenographic plates, many times demonstrate conclusively a condition that would otherwise remain obscure.

Of the patients here studied, seventy-eight were classified as suffering with chronic gastritis. Only those patients have been included here in whom the gastric disease was the only one to be found. The symptoms given were described as, fullness, distention, bloating or a sense of weight or pressure; sometimes this is spoken of as a dull ache but never severe pain.

These feelings are caused by the food soon after it is taken, not after an hour or two of comfort. Next in frequency, complaint is made of belching and of frequent eructations of gas for a long time after meals. As this goes on repeatedly, relief is gradually obtained. Vomiting was found to be a much less frequent manifestation of chronic gastritis than most text-books lead one to expect. On the whole, sour stomach is an unusual feature of this form of gastric disease. Reflex symptoms form a large part of the history and may form so large a part as to distract attention from the stomach itself. Headache, indigestion, depression of spirits, drowsiness particularly after meals, lack of energy, and general indisposition for exertion, are among symptoms recited. Physical examination or roentgenographic plates and fluoroscopic examination are largely negative in this condition. The diagnosis rests on examination of stomach contents obtained after a test meal, which in chronic gastritis gives results which are positive, definite and diagnostic. The amount of gastric juice obtained is small, comes through the tube with difficulty, is very thick and viscid and often semi-solid. An important diagnostic sign of chronic gastritis is the presence of mucus in the stomach contents. The most characteristic sign as regards gastric secretion is either complete an-acidity or decided subacidity, yet cases occur with normal acid values and few apparently with hyperacidity.

At least twenty-five of the author's patients with a total acidity under 10 and no free or combined hydrochloric acid might have been assigned to a separate group called "achylia gastrica," but there seems no particular

object in giving these cases a special name. They all correspond in clinical history, gastric analysis, presence of abundant mucus and negative roentgenographic plates to chronic gastritis; and there appeared to be no reason for assigning them to a separate classification. Not all achylia gastrica cases may originate from chronic gastritis, but as yet we have no proof for any other pathology.

Patients who have been classed as suffering from gastropotosis when asked for details give a story which resembles that of cancer, or ulcer or chronic gastritis, or one of the gastric neuroses. It was found much more common in women than in men. It appeared in small persons, fragile in build and light in weight. Many of them presented other complaints, such as a chronic constipation, pain in the back and right side, inability to put on weight, lack of vitality. Physical examination revealed conclusively the low position of the stomach in the abdomen. In most instances, the acid values of the stomach contents were normal or above normal. The most conclusive proof of the true conditions present is furnished by the roentgenographic plates.

The last group described in this article is that of gastric neuroses. In the first place chronic gastric diseases presenting the characteristics in any of the foregoing groups should be classified as one of them and not a neurosis. A diagnosis of neurosis is not to be made until such conditions as chronic appendicitis and chronic cholelithiasis or chronic cholecystitis or pelvic diseases have been carefully eliminated.

[The greater the number of gastric cases seen by the General Editor the more unwilling he is to make a diagnosis of gastric neurosis. The more intensely each such case is studied the more inevitably it falls into a definite pathologic classification. As the author says, many such cases are due to cholecystitis or cholelithiasis, chronic appendicitis, adhesions, colonic malformations, ptosis of one or more of the abdominal viscera, or even latent gastric or duodenal ulcer. Some have subsequently disclosed themselves as actual carcinomata. The diagnosis of gastric neurosis should never satisfy a careful diagnostician.—GEN. ED.]

Objective Signs of Dyspepsia. In view of the difficulty a military surgeon experiences in deciding whether a man complaining of dyspepsia is a malingerer or not (unless of course the physician has a laboratory at his disposal) has led M. Pron⁷ to a study of the physical signs which may permit the presence or absence of a stomach affection to be determined. The following signs appear to him to be the most characteristic:

1. The appearance of the abdomen and the changes in shape which occur in assuming the erect from the recumbent position, and which depend upon the degree of relaxation of the musculature of the abdominal walls. This relaxation coexists with an analogous relaxation of the gastric musculature.

2. Splashing sounds after meals: a normal stomach does not splash, even when full.

3. Splashing in a young subject indicates a chronic and serious trouble.

4. Dilatation of the pupils on pressure over the pit of the stomach (Leyen's sign) denotes an abnormal irritability of the solar plexus.

These signs the malingerer can not imitate.

Gastroptosis and Gastric Function. A study of the influence of gastroptosis on gastric secretion and motility has been made by A. Everett, James Barnes, and William J. Brooks,⁸ of Boston.

The patients were 127 women of the poorer class, many of whom had borne from six to fourteen children, and who had usually confined their stay in bed after labor to from two to five days.

A study of the acidity of the gastric contents was made by the use of the Carlson water meal. Motility was studied by the usual motor meal method. The determination of gastroptosis in these patients was made by the use of *x*-ray plates, stereoscopic examination in many instances, while in others physical examination alone was sufficient to determine the condition. The authors state that their own results in conjunction with the consensus of opinion of others show:

(7) *Presse méd.*, Feb. 8, 1917.

(8) *Interstate Med. Jour.*, September, 1916.

1. That gastropptosis may exist without symptoms and without any changes in motility or secretion.

2. That the symptoms and changes in secretion and motility do not conform in any way to the degrees of ptosis and further that in the majority of cases secretion suffers, in that a diminution more often occurs while motility is much more rarely affected.

They found that the changes in secretion and presence of symptoms seem to be due not so much to the altered position of the stomach as to nerve influence of central origin, *i. e.*, vagotonus. While symptoms are often relieved by treatment, it is said by way of reminder that the normal position of the stomach is rarely restored, and that the altered secretion is frequently not modified in any way.

A Diagnostic Sign of Gastro-Enteroptosis. In cases of gastro-enteroptosis, according to C. D. Aaron,⁹ deep continuous pressure with the ends of the fingers over the celiac plexus in the epigastrium will induce pain.

The point of sensibility, he says, varies in different individuals, and to locate it the coöperation of an assistant is necessary. With the patient standing, the physician applies his fingers in a series of deep pressures until the point of greatest tenderness is found. The fingers are held at this point. The nurse or attendant then takes a position behind the patient, passes both arms about him so that the hands meeting in front rest on the hypogastrium, and lifts the abdomen in its entirety. This relieves the epigastric pain at once, despite the great pressure exerted by the physician at the point of tenderness. When, however, the nurse allows the patient's abdomen to drop to its former position, the deep pressure continuing, the pain reappears. Aaron states that he has found this sign constant in gastric-enteroptosis. In organic disturbances such as gastric ulcer or cancer the pain pressure continues even when the abdomen is lifted.

[This test is a subjective one. It depends for its answer upon the patient. If the patient is one who readily takes suggestion, the sign is apt to leave one

(9) Archiv. Diagnosis, April, 1917.

wholly in the lurch. This sign will not stand the test of time.—GEN. ED.]

Importance of Duodenal Alimentation in Severe Dyspepsia After Gastro-Enterostomy. In this article, Max Einhorn¹⁰ calls attention to the fact that gastro-enterostomy is the operation most frequently performed in organic diseases of the stomach and that not infrequently after the operation the patient manifests a new train of symptoms which may be just as severe—if not severer—than those existing before the operation. Peptic ulcers in the stomach or jejunum in the vicinity of the new stoma, or adhesions, are the most frequent causes of the new disturbances. The most prominent symptoms are pain, vomiting and hemorrhage. Usually it is possible by thorough examination and careful handling of the situation to ameliorate the symptoms. Liquid diet, large doses of bismuth, and lavage of the stomach are important in the treatment. Occasionally, however, all these measures fail and the physician is at a loss to know what to do. Many of these patients have to undergo another operation, frequently with an indefinite result as to the future. It is in such cases that duodenal or, more correctly speaking, jejunal alimentation, is of great benefit.

Whenever we have to deal with postoperative dyspeptic symptoms of a grave nature, it is best, Einhorn says, to make a thorough analysis of the case with regard to gastric secretion and food retention. Examination with the duodenal bucket is here of great importance. The string attached to the bucket shows whether there is a patent opening leading into the duodenum or jejunum; whether there be ulceration at the stoma, and ultimately whether the bucket has passed through the pylorus or through the new opening.

The presence of a blood stain on the string below eighteen or nineteen inches speaks for ulceration near the stoma. If a yellow discoloration (bile) appears on the string, beginning at about twenty-three inches or further down, it usually indicates that the bucket has passed through the pylorus. If the yellow discoloration begins at nineteen or twenty inches, it indicates

(10) Med. Record, June 16, 1916.

that the bucket has passed through the new opening—for the distance from the cardia to the new stoma is much less than to the pylorus. Should there be a yellow discoloration on the string up at sixteen or seventeen inches, then we remain in the dark as to the patency of either the pylorus or the new stoma. We know only that there is regurgitation of the intestinal contents with bile into the stomach, but we are in doubt as to how far the bucket has gone. In order to clear up this point, *x-ray* examinations with bismuth are required.

In all cases in which the bucket has reached either the duodenum or jejunum, Einhorn says that treatment may be tried with either duodenal or jejunal alimentation. This gives complete rest to the stomach and pylorus, or the new opening, respectively, and so serves to ameliorate the condition.

Within the last few years, Einhorn has treated a number of such cases and has kept track of ten. He cites details of two of these cases and in the accompanying table gives the important points in the other eight.

He summarizes this report as follows:

Eight of the patients treated by duodenal alimentation made a complete recovery, not requiring any surgical aid.

Of the other two, one felt considerably improved during the period of duodenal alimentation, but as soon as the tube was removed and nourishment was given in the usual way the pains returned. A provisional diagnosis of severe adhesions with perigastritis was made, and it was necessary to reopen the wound. The diagnosis was corroborated by the laparotomy, and an anterior gastro-enterostomy was performed.

The other also derived considerable benefit from duodenal alimentation for several months, but the formation of a new ulcer, with hemorrhages, necessitated surgical intervention.

Duodenal or jejunal alimentation is therefore of distinct value, Einhorn believes, in severe post-operative disturbances of the stomach.

[Einhorn's method has been used at Mercy Hospital,

TABLE OF CASES OF SEVERE POST-OPERATIVE DYSPESIA TREATED WITH DUODENAL OR JEJUNAL ALIMENTATION.

Name.	Nature of Operation.	Principal Symptoms.	Gastric Contents.	Duodenal Bucket		Remarks.
				Blood Stain.	Bile Stain.	
1. Elwood H.	Gastroenterostomy, May, 1914.	Severe epigastric pains.	HCL + Acidity = 75 Blood +	19½" - 20½"	26½" - 31½"	
2. Miss Marie H.	1st, gastroenterostomy. 2d, pyloric occlusion, April, 1915.	Gastralgia and vomiting.	HCL + Trace Acidity = 30	15" - 16"	26½" - 40"	Pylorus patent: duodenal bucket, confirmed by X-ray examination.
3. Mrs. H. K.	Gastroenterostomy and pyloric occlusion, Feb., 1915.	Distress after eating and frequent vomiting.	HCL + Acidity = 55	19" - 20"	20½" - 32"	Pylorus patent: duodenal bucket, confirmed by X-ray examination.
4. Solomon S.	Gall-bladder operation, Feb., 1915.	Pains late after meals, also hunger pains.	HCL + Acidity = 100	20½" - 22½"	26" - 29"	
5. Thomas K.	Gastroenterostomy, March, 1916, for perforated duodenal ulcer. Operation No. 2, anterior gastroenterostomy.	Epigastric pain, constant vomiting.	HCL + Acidity = 80 Slight food retention	21"	24" +	Duodenal bucket passed through pylorus; duodenal alimentation for two weeks; during this period, perfect euphoria; when feeding by mouth was resumed, pains returned. X-ray showed tube lying in pylorus and duodenum, no bismuth going through gastroenterostomy. Second operation: Anterior gastroenterostomy.

6. Mrs. Sadie S...	Operation 1913, gastroenterostomy.	Repeated hemorrhages and gastric distress.	HCL + Acidity = 50 Occult blood +	19" -20"	20" +	Duodenal bucket went through gastroenterostomy: ulcer in stomach. X-ray diagnosis: carcinoma. Duodenal alimentation brought benefit for six months; then a new hemorrhage, and again duodenal alimentation was utilized.
7. Archibald S...	1914, gastroenterostomy.	Severe pains late after eating, and hunger pains.	HCL + Acidity = 60	19"	20"	In 1914 operated for gastric ulcer; gastroenterostomy: three months later HCL +, acidity 60; blood stain on string at 19", bile at 20". Severe gastralgia and hunger pains. Duodenal alimentation improves condition. In 1915 gastric hemorrhage: duodenal alimentation again used with benefit.
8. Adolph Z.....	Feb., 1917, operated twice for severe dyspepsia.	Pain, right after meals.	HCL + Acidity = 50	20"	24"	Duodenal alimentation brings benefit.

in Chicago, in a case of persistent hemorrhage from a gastric ulcer. It is infinitely superior to rectal feeding. —GEN. ED.]

Cardiospasm. A consideration of cardiospasm with a report of a case is given by B. B. V. Lyon,¹ of Philadelphia. After a review of the chief contributions to the literature of this subject the author gives a classification of the causes given for cardiospasm as follows:

1. Primary cardiospasm (Meltzer).
2. Primary esophagitis (Martin).
3. Primary atony of the esophageal musculature (Rosenheim.)
4. Functional disturbance of the innervation of the esophagus, due to paralysis of the vagus causing simultaneous spasm and atony of the musculature of the esophagus (Kraus).
5. Congenital disposition (Fleiner, Zenker, Luschka and Sievers).
6. Kinking at the hiatus esophagei (Plummer).

Bassler has called attention to a condition which has no doubt been classified and treated as cardiospasm but which Vincent thinks a spasm of the esophageal opening of the diaphragm due to contraction of the muscular fibers of the crura, which contracts the esophageal opening by drawing the central tendon of the diaphragm against the front of the esophagus, or contracts it at the sides.

The first subjective symptoms are those usually volunteered by the patient, namely, a sensation of discomfort felt behind and usually to the left of the lower end of the sternum. This sensation is variously described as a dull, aching pain, sometimes throbbing, sometimes burning, sometimes cutting, or a sense of pressure or weight. As the condition progresses compensatory hypertrophy of the musculature must develop to overcome the increasing obstruction, and here a second symptom makes its appearance, namely, the regurgitation of foods from the esophagus into the mouth, very shortly after their ingestion, due to the over-active contracting efforts of the esophageal musculature. As food products are retained for longer and longer periods within the esophagus fer-

(1) Amer. Jour. Med. Sci., March, 1916.

mentation and decomposition, chemical and bacterial, take place resulting in secondary esophagitis. At this stage the condition of some patients is truly deplorable; they suffer continually with a sense of burning pressure back of the sternum; they are able to eat only small quantities of food at a time, and their total amount of food ingested and assimilated is so small that they lose weight rapidly; and if not relieved may develop a profound cachexia and die, literally of starvation.

The diagnosis is usually made by the symptom-complex, it is so characteristic. A direct diagnosis can always be made by the use of an esophageal bougie, preferably of the Plummer type, or the stomach tube, or by fluoroscopic study and the Roentgen-ray plate. In using a bougie or tube great care should be practiced in attempting to pass the instrument beyond the obstruction, until the diagnosis of cardiospasm is definitely made to the exclusion of diverticuli, a kinking at the hiatus, stenosis due to malignant disease from within or without the esophagus, or from external pressure by an aneurysmal sac or mediastinal tumor.

To rule out these differential possibilities, when the condition is suspected, the Roentgen-ray examinations should be used first. The following method of diagnosis is offered:

With the tip of a stomach tube in the esophagus at a point just above the obstruction, water is allowed to run in from a graduated glass tank. It will be seen to run much more slowly than if the tube were in the stomach. From 100 to 500 c.c., according to the amount of esophageal dilatation, will run in slowly, but evenly until the flow suddenly stops and the level of fluid in the graduated glass tank begins to oscillate slightly. At this point the water is allowed to escape through the outflow tube, and without changing the position of the stomach tube it will be seen that the amount recovered is equal to the amount introduced.

The importance of diagnosing a secondary or complicating esophagitis and treating the entire condition in such manner as to relieve the infection, is emphasized. Lavage with medicated solutions is recommended by Lyon in the treatment of such infections.

The general treatment of this condition is discussed. In the earlier cases of cardiospasm of the primary type, relief may usually be obtained by the administration of antispasmodics, such as belladonna and atropine, pushed to the limit of tolerance; and with due regard to a possible neurotic etiologic factor, the regulation of proper hygiene, and the use of hydrotherapy and exercise, preferably in the open air, should be advocated. If these measures do not suffice, esophageal bougies may be used or the spastic cardiac ring may be dilated by means of dilators of the types suggested by Plummer and by Bassler.

Patients who are in poor physical condition as a result of prolonged cardiospasm, with severe lesions, may be, at times, best treated by first doing a gastrostomy that feeding may go on while mechanical force is being used gradually to dilate the constricted portion of the esophagus.

The record of a patient who had cardiospasm complicated by esophagitis, and the treatment used, is given. In the treatment it is to be noted that lavage with medicaments, the passage of bougies, and stimulation with the electric current passed through an electrode, introduced into the esophagus through a rubber tube, and liquid diet, were the chief factors. Complete recovery ensued and the diet was gradually changed from a fluid to a semi-solid, and then to a solid one.

Achylia Gastrica. In a critical study of between six and seven hundred cases of all kinds in the gastrointestinal clinic of the Brooklyn Hospital Dispensary, sixty-five, or about 10 per cent., were found by Albert F. R. Andresen² to be suffering from achylia. In private practice the percentage would undoubtedly be lower, he says, because among the better classes there is not seen the neglect and abuse of the body which plays such an important rôle in the etiology of this condition. Nevertheless, probably 5 per cent. of all patients with gastric disturbances would be found to have achylia gastrica if examined. The first study is based upon the sixty-five cases referred to above.

Strictly speaking, the author says, achylia gastrica is

(2) Med. Record, Nov. 11, 1916.

the name given to a condition characterized by an entire absence of gastric secretion; *i. e.*, an absence of hydrochloric acid as well as of the enzymes, pepsin and rennin. By common consent, however, it is now understood that the term includes all cases in which there is an absence of free hydrochloric acid in the gastric contents, although enzymes and some combined acid may be present.

He considers the etiology of achylia gastrica under the headings of "Abnormalities of the Gastric Glands," "Diseases of the Blood" and "Abnormalities of the Nervous System."

Under the first of these headings are considered functional abnormality of the glands; *i. e.*, a condition in which normal glands do not produce normal secretions; further, inflammatory conditions of the gastric mucosa, either a catarrhal condition as a result of chronic irritation, from the ingestion of alcohol or nicotine to excess, or improper or insufficient masticated food; or infective as the result of primary foci of infection elsewhere causing a general inflammatory condition of the gastric mucosa. In the first series of sixty-five cases, 89 per cent. showed infections of the mouth, nose or throat. A third division under abnormalities of the gastric glands is atrophy of the gastric mucosa, as a result of chronic inflammation as noted above; or from arteriosclerosis or new growth pressing upon or destroying the secreting cells, such as carcinoma, sarcoma, fibroma, gumma, or extensive scar tissue from chronic ulcer, also distant wasting diseases, such as tuberculosis, intestinal parasites, chronic malaria, diabetes, plumbism, sprue, pellagra, etc.

Under the heading of the diseases of the blood, Andresen considers anemias and leukemias; pernicious anemia, long recognized as an accompaniment of achylia, has been attributed by some to be the cause, by others, the result of achylia; gouty conditions and intestinal or other toxemias, syphilis, tuberculosis, or any form of septicemia. Diseases of the glands of internal secretion are also mentioned under this heading.

Concerning abnormalities of the nervous system, these are exemplified in tabes, during the crises of which there is as a rule an achylia, and by the still largely theoretical

states known as vagotonia and sympatheticonia. Under this heading are also classed chronic infections; bad teeth; i. e., gross evidences of decay and infection were found in fifty-eight, or 89 per cent., of the sixty-five individuals studied in this series.

A simple explanation of the cause of achylia which the author thinks has not been offered before, would be that, except possibly in congenital cases or in those due to tumor or disease of the glands of internal secretion, it is always due to a chronic generalized hematogenous infection of the gastric mucosa, probably by the *Streptococcus viridans*, as a result of a primary focus of infection elsewhere. Abuse of the stomach, leading to lowered resistance, would be considered an etiologic factor in this direction.

He states that the average duration of the symptoms before the patient applied for treatment was one and one-half years. Pain or distress at variable times after eating were complained of in 87 per cent. of the cases. Sour regurgitation and vomiting, hematemesis, constipation, and chronic diarrheas, were complained of in the frequency of the order in which they are given; anorexia, muscular weakness, insomnia, nervous irritability, were usually complained of. Loss of weight was common but not excessive.

In making the diagnosis of this condition, the gastric contents, removed with the ordinary stomach tube one hour after an Ewald test meal, show an absence of chymification and an increased motility, the mass extracted being thick, moist, and sausage-like. There was also an absence of free hydrochloric acid, a total acidity usually under 20, absence or great reduction in proteolytic and milk-curdling enzymes and the presence of more or less mucus.

In his own work Andresen has used Rehfuß's fractional method of test-meal examinations. In discussing treatment of this condition, the author says first that the removal of any infected foci, which in addition to being a probable etiologic factor in the disease tends to weaken the patient's reconstructive powers so necessary to effect a cure, is of much importance. The treatment of any constitutional abnormality complicated or

possibly acting as a causative factor in the achylia is also to be remembered: anemia, leukemia, malaria, syphilis, tuberculosis, cardiovascular-renal diseases, rheumatic conditions, alcoholism, etc. The author has used a combination of ferric chloride and calcium chloride with hydrochloric acid. Conservation of the motor power of the stomach and the treatment of this condition must be carefully considered. Feedings should be given frequently and in small quantities, rather than to allow the stomach to become over-distended at any time. Mineral oil is given in table-spoonful doses morning and evening; it is soothing to the irritated gastro-intestinal mucosa, and besides being of value in relieving constipation it is not contra-indicated in diarrhea. The following table represents the diet recommended by this author:

Food.	Quantity.	Calories.
Breakfast.		
Apple sauce	4 ounces	75
Milk	6 ounces	125
With cocoa or lactose.....	$\frac{1}{2}$ ounce	40+
Cereal	4 ounces	75
With sugar	1 dram	25
With cream	1 ounce	50
Egg, poached, on toast.....	1 egg, 1 slice	150
Bread and butter.....	1 slice	65
		<hr/> 605
10:30 A. M.		
Milk	6 ounces	125
With lactose	$\frac{1}{2}$ ounce	40
Graham crackers	2 small	10
		<hr/> 175
Lunch.		
Cream vegetable soup or purée.....	5 ounces	125
Milk and lactose, as above.....	6 ounces	165
Bread and butter.....	1 slice	65
Bread or chocolate pudding.....	4 ounces	200
		<hr/> 555
4 P. M.		
Milk, lactose and graham crackers...	As above	175
		<hr/> 175
Supper.		
Potato or tomato bisque soup.....	4 ounces	75
Fresh asparagus.....	1 ounce	25
Raw cabbage salad.....	2 ounces	50
Bread and butter.....	1 slice	65
Milk and cocoa or lactose.....	As above	165
Gelatine with cream.....	4 ounces	50
		<hr/> 430

On Retiring.			
Milk, lactose and crackers.....	As above	175	175
<hr/>			
After Each Meal.			
Olive oil	$\frac{1}{2}$ ounce	134	400
<hr/>			
Total number of calories: 2,515.			

Concerning the use of hydrochloric acid, Andresen believes that the dose should vary from 15 drops to one teaspoonful or more of the dilute acid, preferably beginning with larger doses and reducing their size as the symptoms are ameliorated. It should be given one-half hour after eating, well diluted with water and swallowed through a tube to avoid burning the teeth. He says that enzymes and activators, at one time very fashionable, have now fallen into disuse.

Dietetic Treatment of Gastric Achylia and Resulting Intestinal Disturbance. A. Fischer,³ in his long and interesting article, emphasizes the importance of dietetics in secretory insufficiency of the stomach. He does not believe that to make up the deficit in hydrochloric acid and pepsin is all that is required. It should be the aim of the physician, he says, to influence and restore to a normal level the fine functional inter-play association of the digestive organs, since the manifold and varied symptoms resulting from achylia include not only metabolic disturbances, but also nervous manifestations impairing the general health.

He reviews the history of achylia and gives an excellent bibliography at the end of his article. His assertion is that there is plenty of evidence to prove that achylia gastrica may occur from functional disturbance alone, especially in young persons with a neuropathic or other constitutional predisposition. For example, one of his patients with achylia was 25 years old, and during the ten preceding years had never menstruated since puberty. His investigations lead him to believe that most of those who present gastric achylia are of "low-powered" constitution and that physical inferiority may be congenital or the result of debilitating disease. Depressing nervous influences or abnormal

(3) Corr.-Bl. f. schweiz. Aertze, Sept. 2 and 9, 1916.

composition of the blood, especially in the anemias, may be responsible.

Treatment should be directed to supplying ample nourishment while sparing the stomach or giving it as much rest as possible. Food that is not digested irritates the stomach and sets up a vicious circle with a resultant chronic gastritis developing from what was at first purely a functional achylia.

The symptoms of achylia may be insidious or may simulate hyperchlorhydria disturbances, or achylia diarrhea may be the first warning. The bowel troubles with achylia gastrica need not entail diarrhea, as there may be severe constipation, or the constipation may alternate with diarrhea.

The intestinal digestion of fat, of albumin or of carbohydrates may be defective, but as a rule all three suffer, and the bowels must be spared as much as possible. Buttermilk, whey, kefir and milk sugar render good services here when individualized, as also massage, hydrotherapy, oil enemas, exercise, etc. The meals should be smaller and more frequent, whether the motor function is exaggerated or decreased, *viz.*, hypermotility or motor insufficiency. Milk may cause digestive disturbance with achylia, chiefly because of abnormalities in the peptic, pancreatic and intestinal secretion reactions. Buttermilk, yoghurt and whey are better borne. Since Pavlow has demonstrated that lactic, butyric, acetic and citric acids all stimulate the secretion of pancreatic juice, the use of milk in these forms is logical.

He further allows in the diet soups, especially in the form of bouillons of fowl, pigeon, beef, fish and meat extracts; purée, as of tapioca, sago, etc.; farinaceous dishes, as macaroni, spaghetti and noodles; fresh water fish and salt water, as sole, halibut, salmon, etc.; vegetables he gives only in the form of fine purées. Alcoholic liquors are interdicted, except possibly red wine, and coffee is not commended.

The teeth should be put in order and hygiene of the table enforced, with scrupulously complete mastication. The diet should aim to keep up the strength while sparing the heart and the kidneys to the utmost. When the achylia is due to constitutional physical inferiority, spe-

cial care must be taken not to overtax the organs in giving tonics. Even when achylia results from a physical defect beyond our power to correct, we can adapt our measures to this and strive to compensate for the lacking secretion by calling on the intestinal functions and giving the food in small and frequent meals, mostly in fluid form or soft mashed, with very little, if any, meat, and this tender or chopped fine. Tapioca, rice and meringues may be used to give variety, as indicated in the above diet list. For beverages Fischer allows only tea when the motor functioning is insufficient, and orange flower tea when it is normal, linden flower tea when there is gastrogenous diarrhea, and yoghurt when there is constipation. These beverages are allowed only once a day, at afternoon tea, according to a series of daily menus which are prepared for each individual case.

Treatment of Simple Achylia. The treatment of simple or benign achylia gastrica is divided by William MacLennan⁴ into general and medical. Under the heading of general treatment he says that any obvious adverse hygienic condition should be removed; fresh air, gentle exercise and avoidance of fatigue and over-excitement are essential to success. If there be loss of weight rest in bed and general massage with olive oil have yielded excellent results. This is especially the case in individuals who are distinctly neurasthenic. For these a complete and rigid course of Weir-Mitchell treatment may be followed by rapid progress toward recovery. After the massage, physical culture in the patient's own home should be carried out persistently. Müller's exercises are suitable for most people, and their systematic use improves the nutrition and the gastro-intestinal functions. MacLennan has not been able so far to convince himself that high-frequency or other electrical treatments have had any curative influence.

The outline of diet and its value are much the same here as has been given elsewhere.

Medical treatment, MacLennan says, aims at bringing the gastric glands to a better secretion. Bitters are sometimes useful, but alone are not sufficient. By far the most important therapeutic agent possessed is hydro-

(4) Glasgow Med. Jour., January, 1917.

chloric acid, more especially when it is combined with pepsin. If it be kept in mind that about three pints of gastric juice are normally secreted in 24 hours, and that hydrochloric acid is present in from 0.1 to 0.2 per cent., it will be seen that the dose of dilute acid must be very large. Indeed, it is not practicable to administer all the acids represented in the normal output. In permanent total achylia the administration of hydrochloric acid must be as continuous as is the administration of thyroid in myxedema. But in persons in whom the glands are not destroyed, but only functionally inactive, the gastric contents should be tested at intervals to avoid the possibility of producing an artificial hyperchlorhydria. The dilute hydrochloric acid should be administered in one dose after each of the three principal meals, which should contain all the proteid material that is to be administered in the day's dietary. These three meals should be taken at five-hourly intervals. Starchy material should not form a large proportion of their contents. The carbohydrates should be taken in the intervals—three hours after each meal—and should, as far as possible, be eaten quite dry, any mixed fluid which may be desired taken when the solids are finished.

The author says that the best form in which to administer artificial digestive is as follows:

℞ Acidi hydrochlorici diluti.....	3i-ii
Glycerini pepsini	3ii½
Extracti condurango liquidi.....	3i
Aquæ chloroformi	ad 3vi.—M.
Sig.—3ii, in water, thrice daily after food.	

Strychnine is sometimes useful, with or without physostigmine. In cases in which there is motor insufficiency, as in the achylia with gastroptosis, this combination has been found useful:

℞ Strychninae	gr. 1/24
Physostigminae salicylatis	gr. 1/96
Quininae hydrochloridi	gr. i
Extracti euonymi	gr. 1/4
Gingerine	gr. 1/4.—M.
Ft. pil. mitte tales, 60.	
Sig.—One pill thrice daily after food.	

Gastric Hemorrhage. An account of four cases in which Alexis V. Moschowitz⁵ operated, after unequivocal diagnosis of a bleeding ulcer of the stomach had been made by himself and his colleagues, but in all of which he failed to find any lesion whatsoever when the stomach was examined surgically, is given in detail. It is said that in spite of the most unfavorable outlook in all of these cases, and practically a hopeless one in two, all of the patients have recovered.

The examination of the stomach in each case was made without opening that organ, and therefore the pathologic data are somewhat incomplete.

Under the heading of review of the literature, the author says that previously bleeding from the stomach was thought to have occurred by diapedesis. The generally accepted view now, however, is that all bleeding from the stomach, particularly that of larger quantities, must be the result of a defect in the mucosa.

A study of the author's first observation of gastric material and a critical review of the literature upon the subject lead him to the conclusion that all defects of the gastric mucosa other than neoplastic may be grouped under the following three forms:

The "mucous erosions," so called, accredited to Einhorn.

The "*exulceratio simplex*" so-called, accredited to Dieulafoy.

The "true gastric ulcer" of Cruveilhier.

It is Moschowitz' opinion that the cases here reported belong to the second group, or that of Dieulafoy.

Concerning this lesion known as "Dieulafoy's ulceration," it has been antedated by a number of writers, notably Chiari and Murchison in the report of cases of massive or even fatal gastric hemorrhages, in which the autopsy revealed either a trivial lesion or the entire absence of any lesion, but it was undoubtedly Dieulafoy's masterly and vivid description, and most particularly the recovery of his second patient, after an operation, deliberately undertaken to check the hemorrhage, which has awakened the interest of the medical profes-

(5) Amer. Jour. Med. Sci., November, 1917.

sion to the malady under discussion. Some of the records of Dieulafoy's cases are presented in the original article.

This condition is said to have only one well-marked symptom, namely, profuse hematemesis. This is such a characteristic symptom that the disease may be divided into two parts, (1) before, and (2) after the occurrence of the hematemesis.

Before the occurrence of the hemorrhage the history and physical signs are to all intents and purposes negligible. It is found that in a majority of instances the afflicted individuals have no complaints referable to the stomach. The appetite and digestion are fair, and the general health is so good that there does not exist at any time suspicion of impending danger. Suddenly and without any warning the patient vomits blood. It is rather characteristic that the first vomiting is so profuse that the patient shows systemic signs of bleeding. There are cases recorded in which even the first hemorrhage was fatal.

The physical signs before hemorrhages are not known, for obvious reasons; but in view of the absence of symptoms before hemorrhage it is safe to assume that the physical signs must also be negative.

After hemorrhage has taken place the symptoms and physical signs of the disease are merely those of a profound anemia. Examination of the stomach reveals nothing noteworthy. In the few cases in which the gastric contents were examined, nothing characteristic has been found. In some cases a marked hyperacidity, in some normal values, and in others even a hypo-acidity has been found.

The disease affects most frequently females in the early twenties; but males in the later years of life, and even children, are not immune.

In discussing the pathology of this condition, the author states that Dieulafoy's ulceration extends at one point, at least, throughout the thickness of the mucosa, involves the submucosa, and has eroded a vessel of appreciable size. It is in this characteristic only that we can account for the presence of notable hemorrhages in the latter, and their absence in the former. Neither one of these ulcerations is accompanied by any palpable indura-

tion, infiltration or thickening. When eventually such a lesion heals it does so without any recognizable cicatrix formation, and therefore never causes any deformities in the shape of the stomach. Finally, in true ulceration of the stomach, the defect invades more of the coats of the stomach, even to and through the serosa.

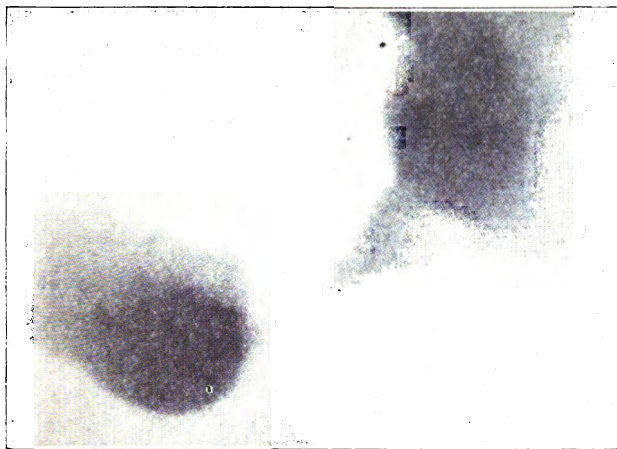
Syphilis of the Stomach. A report of a single case of syphilis of the stomach resulting in hour-glass contraction is presented by R. M. Culler.⁶ The patient was a man 44 years old, who had had a chancre seventeen years previous to the onset of his stomach trouble. He gave a history of a gumma on the shin ten years after the primary lesion. The stomach trouble followed a period of antisypilitic treatment for corneal ulcer. The symptoms consisted of attacks of vomiting, with pain and tenderness in the epigastrium. A diagnosis of gastric or duodenal ulcer was made and the patient sent to the author for operation. X-ray examination following a bismuth meal revealed the condition shown in Plate V, figure *a*. The gastric symptoms were relieved by giving neosalvarsan and mercury, but the patient continued to regurgitate food soon after taking it. Laparotomy was performed and hour-glass contraction of the stomach found, as indicated in Plate V, figure *b*. This portion of the stomach was excised and a complete recovery followed.

Diagnosis of Syphilis of the Stomach. L. T. LeWald,⁷ of New York, says that syphilis of the stomach, whether congenital or acquired, is a rare manifestation of the disease which occurs mostly in males, especially in the fourth or fifth decades. However, it may occur at any age. It is characterized by multiplicity of lesions in many organs, and by variety and plurality of lesions in the stomach itself. The symptoms correspond to the pathologic findings; there is no unanimity of symptoms, though there are four signs which are fairly common, singly or combined. These are: pain, especially after eating, emaciation, tenderness, and hemorrhage. LeWald says that if the Wassermann test is

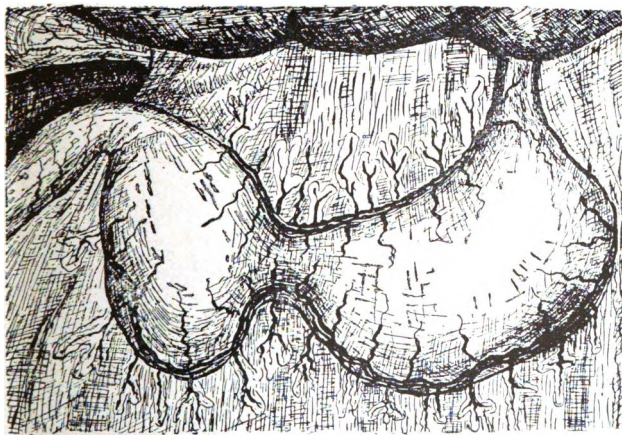
(6) Jour. Amer. Med. Ass'n., Dec. 2, 1916.

(7) Paper read at annual meeting of Amer. Roentgen Ray Soc., September, 1916.

PLATE IV.



Six-hour roentgenogram after bismuth meal, showing narrow isthmus.—R. M. Culler (see page 180).



Appearance of stomach in situ.

positive, or if there is a clear history of syphilis, the diagnosis should be comparatively simple.

[The fact that a patient's blood gives a positive Wassermann or that a patient admits having had a specific chancre does not prove that a gastric lesion is syphilitic. It may or may not be. A therapeutic test raises a presumption that the disease is luetic if the patient gets well, but even such a presumption is, after all, but weak circumstantial evidence. A man with syphilis may easily have a non-syphilitic gastric lesion.—GEN. Ed.]

Diagnosis and Treatment of Syphilis of the Stomach.

B. B. Vincent Lyon,⁸ of Philadelphia, quotes statistics covering a total of 329 cases that came to autopsy, in which 4 instances of gastric syphilis were found, giving a percentage of 1.2 per cent. He says that this estimate will prove far too low, in view of the comparatively large number of cases of gastric syphilis that have been reported in recent years. Further, he declares that it is manifestly a difficult matter to determine accurately the frequency of syphilis of the stomach.

Pathologically the disease may show any one of the following forms: A diffuse gastritis, involving the glandularis and submucosa; syphilitic ulcers, single or multiple, frequently assuming serpiginous forms and having ragged overhanging edges and a smooth base; a diffuse infiltration of the gastric wall which histologically must be distinguished from linitis plastica (unless these conditions are one and the same, as many clinicians believe), from a diffuse scirrhus carcinoma, and from a diffuse infiltration of a tuberculous type; pyloric stenosis; gumma, which may or may not give rise to a palpable tumor.

From a histologic standpoint, the findings are practically those of tertiary syphilis occurring elsewhere.

Under the heading of symptomatology, Lyon says that aside from the comparatively few instances of motor obstruction due to syphilitic pyloric stenosis, the motor defect is much more commonly due to an extreme degree of atony associated with ectasia. The secretory defect is usually accompanied by the symptoms of severe atrophic or sclerosing gastritis. Pyrosis is common and is of

(8) Archiv. Diag., April, 1917.

the type seen in the anacid states; sour eructations, together with the sense of an epigastric lump, weight or pressure sometimes associated with bloating—the symptoms common to atony, together with the fermentations seen in ectasia.

In the ulcer form, one of the early symptoms may be a profuse hematemesis, which is more apt to be recurrent than is common in simple gastric ulcer. In this form there is frequently pain which is more apt to occur late in the day, bears a less striking time relation to meals than is seen in simple ulcers, and is not easily amenable to further food-taking, or to non-specific chemical therapy.

The laboratory findings used as demonstrations showed marked subacidity or anacidity with a greatly diminished or absent enzyme activity. In a few cases the hydrochloric acid contents and peptic activity are normal. There is generally an increase of mucus. The serologic examinations generally yield a definitely positive Wassermann reaction.

By physical examination there are seen the evidences of generalized syphilis as a rule.

Diagnosis as in some other gastric conditions may have to be made by a process of exclusion. The following items are quoted from Morgan:

The failure to glean from the individual anything suspicious of a syphilitic taint, or an abortion, or failure to have children, or a negative Wassermann, does not prove that syphilis does, or does not, exist in that patient.

A diseased condition of the stomach marked by a long duration with changeable symptoms which do not correspond to one or other of the well-recognized diseases of that organ, and which resist the accepted methods of treatment, should arouse suspicion of lues.

Tumors involving the pylorus which do not cause stenosis are more often syphilitic than carcinomatous.

Achylia or a low acidity is usual in gastric syphilis. When there is achylia with symptoms of ulcer, one is likely to have an ulcerating gumma or a superficial ulcer on a syphilitic infiltration base in the gastric wall.

Diffuse syphilitic infiltration is usually easily detected by the palpitating fingers, because it produces some

enlargement of the stomach which, as has happened in some cases, may not be readily recognized at operation. This may be true even when the infiltrating mass can be detected by the Roentgen-ray.

A tumor which does not change its size and shape over long periods of observation may be syphilitic, or a tumor which disappears under antisyphilitic treatment may be presumed to be a gumma.

The treatment of gastric syphilis is practically the same as is indicated in any late secondary or tertiary lesion of syphilis, save those which involve the spinal or central nervous system.

[The symptomatology given by this author can be based admittedly upon but four cases that came to autopsy, and upon a compilation from medical literature of cases described as gastric syphilis, most depending for their diagnosis upon associated lues, a positive Wassermann test, and a few depending for their diagnosis upon cases actually proved to be syphilitic by post-mortem gross and microscopic findings. Until a large series of cases diagnosticated as syphilitic after death by the pathologist has been collected deductions as to a symptomatology differing from that of other analogous gastric lesions is wholly unsafe.—GEN. ED.]

DIETETICS.

Raw Eggs in Dietetics. Working at the Sheffield Laboratory of Physiological Chemistry in Yale University, W. G. Bateman⁹ investigated the usefulness of raw eggs in practical dietetics. In referring to the literature that has accumulated concerning this question, he states that Pavlow, in 1902, observed that the white of eggs had only a feeble ability to stimulate the flow of gastric juice. It acted in this way only as so much water. Cooked egg white, on the contrary, calls forth an abundance of juice and unites easily with the hydrochloric acid.

Referring to the results of a long list of investigators, Bateman says that we may picture this native protein

(9) Amer. Jour. Med. Sci., June, 1917.

then as quickly leaving the stomach, accompanied by scanty amounts of gastric juice and little altered by pepsin. This peculiar behavior is consistently carried on in the intestine, as it has been shown that little or no bile is passed into the intestine after the ingestion of raw egg-white, whereas the same material cooked always caused a good flow of bile.

Once in the intestine, the native egg-white continues to oppose the digestive enzymes, for it has remarkably strong antitryptic properties. It has also been shown that raw egg-white is much more poorly digested than coagulated egg-white by bromelin, the proteolytic enzyme present in the pineapple.

Preliminary heating of the egg-white greatly increases its digestibility by trypsin. Bateman states that this brief review of its properties shows that native egg-white offers such obstacles to digestion as to place it in an exceptional position among proteins. It raises the question as to how the body handles such a substance. Very little upon this point has been recorded up to the present, although raw eggs have enjoyed a great vogue as the mainstay of various diets, especially for the sick.

Experiments consisting of feeding raw egg-white to rabbits and dogs have been carried out and it has been determined that animals fed on this material develop diarrhea, lose weight, and do poorly. Even when the feces appeared normal diarrhea has started; normal undigested egg-white could usually be recovered from them.

In large doses from 30 to 50 per cent. of that ingested was wasted by being ejected with the feces. After the dogs had grown to tolerate this material, as they did after a prolonged time, it was better utilized, but even in these cases the best figure was about 85 per cent. Drying egg-white at low temperatures did not abate its diarrheal activity nor improve its utilization.

When dogs ate cooked egg-white in place of the native or dessiccated protein they did not have diarrhea and the material was excellently utilized, the utilization being in the neighborhood of 90 per cent. When raw and cooked egg-whites were fed on alternate days, or periods,

the difference in the utilization and in the nitrogen balance was striking.

No other native proteins are known to act in the alimentary tract in the manner brought out by these experiments. On account of the importance of the subject from the standpoint of dietetics, it was of interest to determine how raw egg-white comported itself when ingested by man. A number of instances are cited in which individuals took some amount of raw eggs either by direction or as an experiment to test the effect on the intestinal canal. In practically every case there was some laxative effect and in many instances an actual diarrhea occurred. The experiments so far described were made with egg-white from the egg of the common fowl, but that it is not unique in its unusual behavior in the alimentary tract was shown when the egg-white from the egg of the duck was found to act in exactly the same manner.

In contrast to egg-white egg-yolk was found to be well digested and utilized.

These experiments show, the author believes, that raw egg-white is a decidedly indigestible substance and that it may cause diarrhea and vomiting when ingested in any large quantity. Its utilization by the body is poor, since it is used only to the extent of from 60 to 70 per cent. A series of long quotations from familiar names in literature of the past is given, to show the reason heretofore underlying the use of raw eggs, and Bateman shows that these are not based upon the sound principles that have been worked out in the present work. The results of the present study show these to be not well-supported and indicate that raw egg-white is decidedly inadvisable.

A substance which fails to stimulate a flow of gastric juice, is anti-peptic, which hurries from the stomach, calls forth no flow of bile, and strongly resists the action of trypsin, which is poorly utilized and may cause diarrhea, has evidently little to recommend it as the food stuff of preference for the sound person, not to mention the invalid. And when the native protein needs only to be coagulated at 70 degrees C. in order to

obviate almost all the effects mentioned there appears still less reason for using it uncooked. It is true that fairly large amounts of raw egg-white need to be ingested for the abnormal digestive effects to be made manifest; but even if small quantities are used certain disadvantages may follow. The indigestible protein may reach the large intestine and there become a good pabulum for the putrefactive bacteria. Or mixed with other food it may retard the digestion and lower the utilization of other proteins. Again, it seems more than a coincidence that of all the proteins, the egg-white is the most indigestible and at the same time the most common cause of anaphylaxis. According to the latest views on this subject as stated by Wells (1914), anaphylactic intoxication is caused by the entrance into the blood of intact, foreign protein molecules. If this be so, it would appear that egg-white is a substance peculiarly apt to be the agent in allergy. It leaves the stomach practically unchanged so that in the intestine it may be absorbed still intact or only slightly altered. The strong antitryptic action it possesses leads to the same danger.

Bateman also refers to the use of egg or egg albumin in the rectal feedings made at times by certain physicians, and says that more recent studies of rectal alimentation tend to show that the amount of protein which can be utilized in this way is unimportant compared to the requirements of the body.

In conclusion it must not be assumed from the foregoing discussion, the author says, that native egg-white is considered a toxic or otherwise dangerous substance. But the evidence regarding its behavior in the alimentary canal is taken to show that no advantage accrues to the body by using it raw rather than cooked. Furthermore, when the diet of those seriously ill is considered it may fairly be asked in the light of scientific evidence if the current extensive use of the raw eggs is not illogical and inadvisable.

Vitamines in Nutrition. In a paper on this subject

(1) New York Med. Jour., June 10, 1916. See also article on "Beriberi," page 132, this volume.

Casimer Funk¹ of Cornell University Medical School states that recently sufficient evidence has accumulated to warrant the statement that beside the ordinary food constituents, such as proteins, fats, carbohydrates, lipoids, and other inorganic salts to the presence of which, with the exception of salts, the caloric value of food is due, a number of substances can be found in very small quantities which are as indispensable to life as the former constituents. These substances are elaborated in both the higher and lower plants, but can not be synthesized by the animal organism, and this is one of the reasons why animal life depends on plants. These products are present in all food, in all organs and in all vital parts of the plant without a single exception. Their presence has been revealed by the modern technique of cooking and by the refinement of food due to the introduction of machinery for the industrial preparation of foodstuffs on a large scale.

While beriberi is said to be due to feeding on polished rice, another origin of the disease is from such refined foods as sago, tapioca, or white bread (especially when cooked with baking powder) consumed in disproportionately large quantities, or if subjected to prolonged boiling.

While vitamins have not been prepared as a definite substance, extracts from foods have yielded a substance that cures beriberi in pigeons.

All that is known of the nature of the action of vitamins is that they bear a certain relationship to carbohydrate metabolism. If a pigeon is fed on polished rice it is possible to estimate approximately when the symptoms of beriberi will appear after a given quantity of rice is metabolized. The author has confirmed this with an artificial diet composed of variable amounts of carbohydrates, and it was also found that the blood sugar content in avian beriberi was greatly increased. The fact has a practical bearing in infant-feeding; it must be borne in mind that a certain amount of vitamin can take care of only a limited amount of carbohydrates and when the starch is increased in the diet the amount of vitamin-containing food-stuffs must be increased in proportion.

A second fact which has been established in connection with the metabolism in deficiency diseases is that in the absence of vitamins there is not only negative nitrogen balance, but the whole metabolism goes wrong; this is particularly noticed in the negative balance of inorganic constituents like calcium, phosphorus, and sulphur. Schauman has recently shown that the addition of vitamins puts the whole metabolism again on a normal basis and this fact is of special importance for the understanding of certain conditions like rickets in children. The author also found further that vitamins, when properly prepared and added in sufficient amount to polished rice, makes the latter diet complete. It has been shown, in addition, that no animal is yet found able to live more than a short time on a vitamin-free food and that an artificial diet composed of casein, starch, fat, sugar, and all the necessary salts will produce a deficiency disease of some kind according to the animal chosen, provided that sufficient care be taken to purify the ingredients. To this diet all known lipoids, cholesterol, various proteins, and all sorts of salts may be added and nothing will save the animal or man from certain death unless vitamins be added.

Comparative Value of Lard and Butter Fats in Growth. In the opinion of C. Funk and A. B. Macallum,² the failure of rats to grow on a lard and yeast diet is partially due to the development of scorbutic symptoms. To a marked degree, these symptoms may be relieved by using moist instead of dry yeast and by combining the moist yeast with butter. Even on this latter combination, however, the existing deficiencies are not wholly overcome, and some rats decline on this diet. Rats which fail on lard do not always recover when butter is substituted.

It seems also possible, the authors say, that yeast on account of its high content in purins, and perhaps other constituents, is not an ideal addition in experiments of long duration, even in spite of its marked growth-promoting power. The impaired nutritive value of heated casein does not seem to be due to destruction of amino-acids but to destruction of vitamins.

(2) Jour. Biol. Chem., October, 1917.

GASTRIC AND DUODENAL ULCER.

Practical Pathology of Peptic Ulcer. J. Ewing,¹ of New York, says that opinions regarding the frequency with which cancer develops on ulcer of the stomach vary from 5 to 70 per cent., a discrepancy which suggests that the criteria of this condition are not clearly recognized or employed in diagnosis. The available data bearing on the matter are statistical, clinical, anatomic and microscopic. Statistics show, he asserts, that healed ulcers are common at necropsy; the chief age of incidence of ulcer is between 20 and 30 years, and of cancer between 50 and 60 years; ulcer is much more common in females; cancer is more frequent in males, and the common sites of ulcer and cancer are not identical.

Clinical observation shows that a history of ulcer long precedes cancer in the typical cases; that cancer has followed gastro-enterostomy for ulcer no more frequently than after resection of the ulcer, and that about 2 per cent. of ulcers long treated medically develop cancer. The anatomic appearance of undoubted cases of ulcero-carcinoma has usually been characteristic, the cancer beginning at one point of the ulcer and leaving the base free.

Microscopically, there are a moderate number of cases of chronic ulcer which show suspicious pre-cancerous changes, but these may not safely be regarded as equivalent to cancer. The great majority of chronic ulcers, he thinks, are free from such changes.

Symptomatology and Diagnosis of Peptic Ulcer. This subject was considered by G. E. Lockwood, in a paper read before the Medical Society of the State of New York.² He said that to make a correct diagnosis is laudable, but to make it hastily is culpable; yet this is constantly being done. The Roentgen ray is of great importance but Lockwood emphasizes that it has its limitations. In duodenal ulcer he considers it disappointing and he is inclined to discard its evidence in

(1) Paper read at annual meeting of Med. Soc. State of New York, Utica, April, 1917.

(2) Annual meeting held at Utica, in April, 1917.

that condition. The string test he says is unreliable and often seems to show ulcer where none exists, and fails to show it where it does exist. Gastric analysis may or may not be of service. A double test should be made; one on the empty stomach early in the morning for hypersecretion, and the test breakfast for hyperacidity.

The general characteristics of ulcer are hunger pains and relief after eating. These symptoms are often present in chronic appendicitis also, but it will be found, by careful charting of the regularity of these pains, before breakfast, lunch, dinner and bed, and the time of relief by food, that in the long run chronic appendicitis varies from the clock-like regularity of ulcer; pain overlaps a meal, or lasts all day, and careful watching and charting will make the differential diagnosis. The only confusion which exists is that in late ulcer there is continuous pain with vomiting of sour acid fluid. This is especially characteristic of ulcer. The diagnosis, however, is not easy to make; it requires time, patience and careful checking up by laboratory data. Only operation makes the final diagnosis absolutely certain, and even then the question is frequently reopened by the pathologist's report.

Etiology of Duodenal Ulcer. C. A. Roeder,³ of Omaha, says that traction on the bulb or first portion of the duodenum when the dilated segment or stomach is filled may be a factor in the etiology of duodenal ulcer. The first portion of the duodenum or bulb suspends more weight after meals than any other portion of the gastro-intestinal tract at any time, with the possible exception of the area surrounding the cardiac orifice.

After eating there is constant traction on this part of the duodenum for a period of one or two hours, particularly in individuals who are unable to lie down for an hour after a hearty meal. Roeder says that during the spring and fall the laboring man works hardest and eats most, going to work on a full stomach, with considerable traction on the bulb. The author

(3) Neb. State Med. Jour., September, 1916.

suggests that this may account for the seasonal exacerbations of this disease.

Diagnosis of Duodenal Ulcer. In a review and discussion of the literature and a report of his own experience with duodenal ulcer, A. Everett Austin,⁴ of Boston, states his opinion that the incidence of this lesion is increasing. The evidence in favor of this view is seen in the reports of long series of autopsies.

"For instance, under Chiari, in 3,061 autopsies, duodenal ulcer was found in only 1.38 per cent. Fenwick reports that in 13,055, only thirty-four such ulcers were discovered, or 0.26 per cent. Perry and Shaw report that in 17,652 autopsies, only seventy ulcers, or 0.5 per cent., were found. Weir, of New York, publishes the results of 1,000 autopsies in which only two duodenal ulcers, or 0.2 per cent., were found. In general, upon averaging these and other results, we find 0.365 per cent. of duodenal ulcer. On the other hand, since operation has been more freely undertaken for this disease, based on as complete evidence as could be deduced from symptoms and physical examination, its frequency has steadily increased. Moynihan reports operation in 187 cases in 1908-9 and 115 cases in 1909-10. William J. Mayo reports 152 cases previous to 1906, and 401 from 1906-1911. Why the section statistics should differ so from those obtained by examination *in vivo* has no plausible explanation."

In a summary based upon the factors presented here, Austin says that a diagnosis of duodenal ulcer must be based largely on the four factors of periodical and characteristic fasting discomfort, if not pain; on the presence of hypersecretion, particularly of the alimentary variety rather than the continuous; on the presence of occult blood in the stool; and on distortion of the first part of the duodenum, as shown by the radiogram. A short perusal of any series of case histories will soon show that all of these are practically never found in any one case. When, however, any two or three are evident, we may well forego the presence of the fourth factor. The relative value of the history, of the char-

(4) New York Med. Jour., Nov. 18, 1916.

acter of the pain and its intermissions, and the detection at some time of occult blood in the stool, appears to him to be of the greatest importance. On account of the close similarity of symptoms of duodenal ulcer and functional hypersecretion, the former lose much of their significance and dependence must be placed more on physical signs than on symptoms; and, as hypersecretion is present both as a functional disorder and as the outcome of ulcer, we are driven to the conclusion that occult blood in the stool and the distortion of the duodenum shown by the *x*-ray examination are the positive signs on which we must largely base our diagnosis.

So far as the differential diagnosis is concerned, there is probably no condition which so closely simulates duodenal ulcer as cholelithiasis. Reference is not made by Austin to the typical attacks of gall-stone colic with vomiting, but to the advanced forms, where adhesions have taken place between the gall-bladder and the duodenum. It is common, too, to find in cases of the gall-bladder involvement, by reflex action, the same hypersecretion which we may find with the ulcer, and, secondly, there is often the tender point so characteristic of the latter. The periodicity of attacks of cholecystitis is well known. In Austin's experience, one of the most distinctive points of difference between these two conditions is the slight trace of bile found in the urine when the common duct and gall-bladder are involved. Still, with the greatest effort at learning the truth, mistakes are often made.

The distinction between gastric ulcer situated near the pylorus, and duodenal ulcer, is often impossible; the author considers it a mere refinement of diagnosis to reach such a decision, and therefore refers to the condition as gastro-duodenal ulcer, leaving differentiation to the surgeon. The ulcer on the gastric side of the pylorus has been found in this work to produce gastric stasis either through the redundancy of the scar tissue or by means of the pyloric spasm which so often accompanies it. As to the delayed pain, or fasting discomfort, there is little or no difference whether the ulcer is inside or outside the pylorus. This does not exclude the possibility of the ulcer being of gastric origin when

it is situated in the lesser curvature or in the fundus, where, unquestionably, pain occurs much earlier.

Diagnosis of Gastric and Duodenal Ulcers. In this article Dahl¹ tabulates the findings in forty-one operative cases, comparing them with the symptoms previously observed, the stomach-content findings and other details.

In nineteen cases there had been no bleeding except occult in two, but all except six of the patients suffered from pain coming on from two to four hours after eating. In these six the pain commenced in from one to two hours; in none did the pain come on earlier than an hour. The pains appeared always at the same point and after the same interval, but the interval was shortest after a small meal and longest after a heavy meal. There was no tender point on pressure in many of the cases, and at times this proved misleading. In a number of patients also there was tenderness only during the periods of pain.

There was hypersecretion in only eight cases, and no vomiting in twenty-three of the forty-one cases. Vomiting occurring at the height of the pains is characteristic, but rare. The Roentgen findings were not decisive in the four cases examined.

In short, Dahl says, the pain is the only constant and reliable symptom of gastric or duodenal ulcer, but this is so characteristic that there can be no mistaking it.

The patients were of both sexes, from 18 to 60 years old; the symptoms suggesting ulcer dated from one to thirty-seven years before. In one case of extensive hemorrhage from the stomach, but no pains, operation failed to reveal any tendency to ulcer, as also in another case of pains without bleeding. In another case the trouble proved to be a cancer in the lesser curvature. The duodenum proved to be sound, although it showed a "*nische* shadow" on roentgenoscopy. Dahl adds that about every sixth one of his patients last year presented symptoms of a gastric or duodenal ulcer, but only a small percentage of them were given surgical treatment. He believes that these ulcers often escape detection. The first signs of trouble develop usually between the ages

(1) Hygiea, 1916, Vol. 78, No. 18.

of 20 and 30. The sooner the ulcer is given proper treatment, the better the result.

Medical Treatment of Peptic Ulcer. Dr. Ludwig Kast,² of New York, says that it is necessary for the physician to understand clearly which patients should be treated medically and which should not.

"Surgical with delay" are (1) cases of perforated ulcers, and (2) repeated serious hemorrhages. "Surgical as soon as feasible" are (1) chronic ulcers, needing preparatory, rigid medical treatment; (2) indurated ulcers; (3) penetrating ulcers and hour-glass contractions, and (4) cases offering suspicion of malignancy. "Borderline cases" (1) with no facilities for medical treatment; (2) neurasthenic cases, particularly those dependent on anodynes.

The condition in all surgical cases is improved by previous medical preparation.

Medical treatment is directed chiefly toward reducing gastric secretion and neutralizing hydrochloric acid as much as possible. Some points in the treatment are: covering and protecting the ulcerated surface by use of bismuth; giving of acid-binding foods; giving of alkalis; checking of gastric secretion; by proper arrangement of diet, avoidance of foods that stimulate gastric secretion. If after several weeks of medical treatment the patient is still dependent on a restricted diet, surgical treatment should be resorted to.

[Covering and protecting the ulcerated surface by the use of bismuth is a fairy story. The bismuth does not adhere to an ulcerated surface at all. This has been abundantly proved both by careful fluoroscopic examination, well-prefaced skiagrams, and particularly by inspection of ulcers at the time of operation by such good observers as W. J. Mayo and J. B. Murphy.—GEN. ED.]

Roentgen Rays in the Diagnosis of Gastric and Duodenal Ulcer and Gastric Cancer. I. H. Levy,³ professor of medicine in Syracuse University, states that it can not be too strongly emphasized that the Roentgen ray

(2) Paper read at annual meeting of Med. Soc. State of New York, Utica, April, 1917.

(3) *Archiv. Diagnosis*, October, 1916.

should not be invoked as a first aid, nor should its evidence be contrasted with the clinical evidence. The x-ray examination should always be part of the general clinical examination. It is nothing more nor less than interior inspection. The fact that it requires special apparatus, and some technical knowledge, in no way removes it from the domain of clinical medicine to a specialty. The author states that it is safe to predict that in the future every physician will be trained to interpret both the fluoroscopic and radiographic shadows.

In discussing gastric ulcer he says that in some cases, especially in the very superficial ulcers, the x-ray findings may be negative. Among the anatomic signs, the incisura is sometimes encountered with ulcer. It results from a spasmodic drawing-in of the wall of the greater curvature. When present it is quite constant; it may be relaxed, however, with atropine. In chronic gastric ulcer with pyloric obstruction the stomach is enormously enlarged, and owing to atony the opaque meal drops to the bottom of the organ. The peristaltic waves are usually shallow, although in some cases they may be exaggerated as the result of hypertrophy of the walls. There is a marked disturbance of the motor function, the bismuth sometimes remaining in the stomach for days. The rest of the stomach is half-moon shaped, and considerably to the right. He refers to the "*nische*," which was first observed by Haudek. It is found in chronic ulcers with a crater, and particularly in the ulcers that have penetrated into the neighboring organs like the liver or pancreas. When the crater of the ulcer is still within the stomach wall, it shows itself a small bud projecting outward from the main bismuth shadow. It is usually found on the lesser curvature. When the ulcer has penetrated into the liver or pancreas, forming the so-called "*ulcus penetrans callosum*" of Haudek, there is a large pocket in which the bismuth settles and remains. An hour-glass stomach is not infrequently encountered with ulcer, even without the "*nische*."

Hypomotility as a sign of gastric ulcer is emphasized. It is said to be always present in the florid ulcer. The delayed emptying is not necessarily due to the pyloric obstruction, but to the reflex spasm of the pylorus.

The anatomic signs of duodenal ulcer are: first, a deposit of bismuth in the center in the crater of the ulcer, which is rarely encountered; and second, a constant deformity of the cap. The suggestive signs are hyperperistalsis with or without a six hours' rest, hypermotility, pain point, hypertonus and reflex gastrospasm.

In duodenal ulcers the stomach is usually small and hypertonic. Even with obstruction this is relatively true, strongly contrasting with ulcers at the pylorus with obstruction in which the stomach is enormously dilated. A pain point is usually encountered in duodenal ulcer. On pressing over the bulbus duodeni while flouroscoping pain is elicited. This, however, is not always present. Pylorospasm and incisura, or abnormal drawing-in of the greater curvature, has also been observed with duodenal ulcer.

Concerning cancer of the stomach, the principal radiologic sign is the filling defect produced by the growth encroaching on its lumen. There is absence of the bismuth shadow corresponding to the location of the mass. An extensive defect in the pars media may produce an hour-glass contraction. In the colloid or infiltrating cancer, the lumen of the stomach is very small; the pylorus, owing to the growth infiltrating its walls, is like a rigid tube constantly open. As a result the stomach empties itself very rapidly. In no other gastric condition do we find so marked hypermotility and beautifully filled coils of small intestine. The food seems to run directly into the latter.

Concerning syphilis of the stomach, the author says that the radiologic signs of this condition are practically the same as that of cancer. In all doubtful cases a Wassermann test should be made and in some, even though that is negative, the patient should be given the benefit of the therapeutic test.

In conclusion, he urges that the Roentgen examination should not be given until a careful history has been taken and a complete physical and laboratory examination made. And when made, its findings should form a part of the diagnostic chain. Should there be any contradiction of evidence, great care must be used in coming to a conclusion.

Prognosis of Duodenal Ulcer. In discussing this phase of the ulceration Max Einhorn⁴ states that great advances have recently been made in diagnosis as well as in treatment. The outlook, therefore, for patients suffering from a duodenal ulcer is now brighter and more favorable than in former years.

Simple duodenal ulcer: Here the usual symptoms are epigastric distress two or three hours after meals; sometimes hunger pains; long periods of euphoria alternating with comparatively short periods of suffering. Gastric hemorrhage or melena may have occurred once. This group gives a comparatively good prognosis, provided that some form of rest cure is rigidly carried out. The oftener the attacks recur the more doubtful the prognosis becomes as to a complete cure by medical measures. Operative intervention (gastro-enterostomy, preferably with pyloric occlusion) offers a pretty good prognosis with regard to the future.

Duodenal ulcer accompanied by pylorospasm and also hypersecretion (alimentary or continuous): Severe pains and frequent vomiting are here the chief symptoms. Hypersecretion, either alimentary or continuous, is also constantly encountered. The gastric juice is usually hyperacid. When the pylorospasm reaches a higher degree slight isochymia appears off and on. The prognosis of this group is not very good under ordinary methods of treatment (alkalies, even milk diet). Duodenal alimentation gives a better prognosis.

Duodenal ulcer accompanied by pyloric or duodenal stenosis: Isochymia is here constantly present. In cases of beginning pyloric stenosis, duodenal alimentation and then stretching of the pylorus may be tried. The prognosis under this mode of treatment varies in different patients. Should there be no improvement, or in case the stenosis is so advanced that the duodenal bucket fails to pass through the pylorus, an operation (gastro-enterostomy) should be performed. Barring the dangers resulting from the surgical intervention, the result is here usually very good, and the prognosis accordingly favorable.

Duodenal ulcer with periodically recurring hemor-

(4) Med. Record, Feb. 10, 1917.

rhages: In this group the predominating symptom is a profuse hemorrhage [either hematemesis or melena or both], which periodically returns, and endangers the life of the patient. An interval operation (gastro-enterostomy, eventually with pyloric occlusion) gives the best results, and renders the prognosis more favorable.

The Influence of Gastric Juice on Gastric and Duodenal Ulcers. A series of experiments on dogs, performed by Lester R. Dragstedt,⁵ in the Hull Physiological Laboratory of the University of Chicago, was undertaken to determine the effect of gastric juice on the rate of healing of acute gastric and duodenal ulcers. He says that it is well known that lesions of gastric and duodenal mucosa heal readily in the presence of active gastric juice. Small abrasions of the stomach mucosa, such as those following at times the administration of a stomach tube, are common, occasion no discomfort in the individual and, in the majority of cases, heal without further sequels. Surgical operations in which there is a maximum insult to the mucosa cells are not commonly followed by untoward effects due to the digestive activity of the gastric juice.

Nevertheless, up to the present, he says, the medical and surgical treatment of gastric and duodenal ulcers has been based essentially on the theory that the gastric juice induces chronicity of these ulcers by digesting the exposed edges of the mucosa.

To produce the ulcers for experimental study a 5 per cent. solution of silver nitrate was injected into the gastric mucosa. Some of these were introduced into Pavlov pouches produced in the stomach of the dog. Some were arranged in such a manner that the gastric juice was always present on the ulcer produced, and others were arranged so that the juice was kept off the experimental organs as much as possible. Ulcers produced in the duodenum were also made in such a manner that the presence or absence of gastric juice upon them could be controlled. The brief of these results as given by the author is as follows:

The average time required for the healing of the experimental ulcers in the Pavlov pouch, arranged so that

(5) Jour. Amer. Med. Ass'n., Feb. 3, 1917.

there was at all times a quantity of gastric juice in the pouch, was eight days.

The average time required for the healing of the ulcers in the pouches in which there was a maximum drainage for the gastric juice was nine days.

The average time required for the healing of the experimental ulcers in the duodenum, both in the presence and in the absence of acid chyme, was twenty days.

Animals killed and examined at necropsy before the ulcers in the duodenum were completely healed showed ulcers in practically the same stage of healing in both cases.

Bacteriologic examination of the ulcers in five of the dogs showed a hemolytic streptococcus in pure culture in two cases, mixed staphylococcus and streptococcus in one case, *B. coli* in one case, and *B. subtilis* in one case. The examination was made with the technique of Dr. E. C. Rosenow.

In commenting on this work, the author states that from the experimental evidence obtained, it would seem that the digestive action of the gastric juice is not the important factor in the delayed healing of acute lesions of the stomach and duodenum, and the consequent production of chronic ulcers. Acute lesions of the mucosa of the stomach and duodenum do not require any longer time for healing, or display any greater tendency toward chronicity when exposed to gastric juice of normal acidity and pepsin strength than do similar lesions in the absence of gastric juice.

Gastric and duodenal ulcers are, therefore, Dragstedt asserts, locally infected areas of the wall of the digestive tract, irrespective of whether the ulcers themselves are produced by primary infection from the blood-stream, by local circulatory disturbances, or by mechanical factors acting on the mucosa from the lumen of the intestine. It is well known that the tissues surrounding the ulcers are hyperemic. It is highly probable that in these hyperemic ulcer areas the nerves (sensory and motor) become hyperexcitable, as in all other areas of infection. These hyperexcitable gastric nerves, subjected to stimulation by the normal gastric juice, may thus yield exaggerated responses (motor, inhibitory, and con-

scious). Carlson suggests that the favorable results from the alkaline and frequent feeding treatments in these cases may be due to the removal of this added stimulation of the hyperexcitable nerves rather than the prevention of any digestive or corrosive action of the pepsin-hydrochloric acid on the tissues. The degree of reflex disturbance from the acid stimulation of the nerves in the ulcer areas would vary with the individual, depending on the severity and extent of the infection, as well as on the individual stability of the entire nervous organization.

The conclusions reached by the author are: The digestive activity of gastric juice is not the important factor in the delayed healing of acute ulcers of the stomach and duodenum and the consequent formation of chronic ulcers. Ulcers produced by local injection of solutions of silver nitrate become subsequently infected with organisms probably from the alimentary tract.

Gastric Ulcer Produced by Injection of Staphylococcus Pyogenes Aureus. These experiments were carried out by E. C. Steinharter⁵ of Cincinnati.

The organisms used were obtained from two patients, one of whom suffered from septicemia and the other from an acutely inflamed appendix. The primary cultures in both cases were made in ascites dextrose broth, and yielded the staphylococcus in pure culture. An emulsion of the staphylococcus which was isolated from the appendix produced, on intravenous injection into rabbits, without any preliminary animal passage, stomach or appendiceal lesions in four out of five rabbits injected. On the other hand, the strain of staphylococcus obtained from the case of septicemia was not, when freshly isolated, of the proper grade of virulence to produce gastrointestinal lesions when injected intravenously into animals, but later, after the organism had undergone preparatory cultivation in the functioning stomach wall of the rabbit, intravenous injection of it was then followed by the formation of gastric ulcer. The ulcers formed were in most cases single. They occurred invariably in the pyloric end of the stomach or duodenum. They varied in size from that of a pinhead to 5 by 7 mm.

(5) Boston Med. and Surg. Jour., March 29, 1917.

In some cases they were punched out, clean and well circumscribed, and in other cases, merely necrotic, bleeding areas. In some experiments the ulcer was the sole lesion, while in others it was associated with appendicitis, cholecystitis and arthritis.

Duodenal Ulcer and Tetany. A single instance of duodenal ulcer in which tetany occurred is reported by Rene Bine⁶ of the University of California Medical School. The patient was a man of 28, with a history of ulcer, and with fairly typical symptoms. He would not be placed on accurate and well-controlled management nor would he consent to surgery until there was an onset of the symptoms of tetany characterized by intermittent, bilateral, painful muscular contractions of the upper extremities, during which his hands assumed the typical tetany position. His stomach was washed, and 1,700 c.c. of greenish fluid removed, with relief of symptoms.

His condition improved and symptoms of tetany disappeared, but returned. A gastro-enterostomy was performed and the patient died on the following day. At autopsy a chronic duodenal ulcer and considerable pyloric stenosis were found. The recent wound was in good condition, and the only other noteworthy changes were those subsequent to poor nutrition.

In his comment the author states that it is probable that the tetany increases the pyloric spasm, or in many cases directly brings it about. Hour-glass contractions have been observed during attacks of tetany in patients whose stomachs were apparently normal at other times and who never presented symptoms suggestive of ulcer. These belong to a second category, that is, those whose gastro-intestinal disturbances occur at or after the outbreak of the tetany, these disturbances being, as it were, but one symptom of the tetany.

The conclusions drawn are that tetany may occur in cases of gastric dilatation associated with pyloric spasm or stenosis.

It may occur most unexpectedly, and in spite of fairly close observation.

The prognosis in any case of gastric tetany is bad.

(6) Jour. Amer. Med. Ass'n., May 5, 1917.

The mortality is greater in cases treated medically than in those treated surgically.

It would seem wise to operate at once in the presence of symptoms of tetany of presumably gastric origin. The surgical procedure would depend on the lesions found.

Medical measures should be instituted after the operation.

Medical Treatment of Duodenal Ulcer. This subject is discussed by W. A. Bastedo⁷ of New York. The following treatment is given in cases with severe hemorrhage: "Secure physical and mental quiet by avoiding as much as possible physical examinations and excitement, and by having the patient lie flat on his back, without pillow, and with an ice-bag over the epigastrium."

The author thinks that morphine not only quiets the mind, allays restlessness and diminishes the chances of vomiting, but it also lessens the tone of the general stomach muscles, induces closure of the pylorus, and thus assists in keeping the duodenal region free from gastric contents for the time being. Nothing should be given by mouth, not even a teaspoonful of water or cracked ice. Thirst may be allayed by the rectal administration of a pint of warm saline solution or tap water.

If the patient is exsanguinated, 1,000 or 1,500 c.c. of normal saline should be administered by hypodermoclysis or by venous infusion; contrary to the general belief, this does not lessen the coagulability of the blood. If it is possible the best procedure would be the transfusion of blood. If the hemorrhage appears to be continuous one may inject subcutaneously every six hours, for three doses, 20 or 30 c.c. of human horse, or rabbit serum; or give intravenously 20 c.c. of a freshly prepared 10-per cent. solution in normal saline of coagulen or coagulose, the so-called "solid serums." The calcium salts are probably of little or no value.

As a rule, surgery is not indicated at the time of the hemorrhage from a duodenal ulcer, because usually the hemorrhage ceases spontaneously or as the result of the measures applied. Subsequent treatment consists of

(7) New York Med. Jour., March 17, 1917.

keeping the patient in bed and allowing nothing by mouth for about three days, which, however, is an arbitrary length of time. For thirst, rectal injections of from one-half to one pint of saline or tap water may be given every four to eight hours or a Murphy drip of saline or tap water at twenty to sixty drops a minute, *i. e.*, two and one-half to seven and one-half ounces an hour. The bowel is cleansed by a daily soap-suds enema. It is especially desirable that all blood should be passed from the intestines, as otherwise it is prone to putrefy rapidly. A nutrient enema may be given, if considered desirable, two or three times in twenty-four hours. It is necessary that plenty of water be administered, but it is probable that the small number of calories that can be made available by rectal feedings will be of very little benefit.

When there is no severe hemorrhage, or after severe hemorrhage has ceased for at least three days, treatment is as follows: "If the case is definitely surgical there is no use wasting time on the medical treatment. The treatment is considered surgical if there is acute perforation; if there is chronic perforation as demonstrated by Roentgen rays; if there are adhesions as demonstrated by Roentgen rays; if there is pyloric obstruction; if there is suspicion of carcinomatous change. It is true, cancerous change is very rare with duodenal ulcer, but one can not always be quite sure that the ulcer is duodenal and not prepyloric. If, in spite of proper medical treatment, it is the site of repeated copious hemorrhages or of persistent bleeding, even in small amounts, or if it is a constant source of pain or nausea, or if it interferes persistently with nutrition, operation should be performed."

Rest is obtained by keeping the patient in bed for a period of three to four weeks, then allowing him to sit in a chair, say twenty minutes the first day, and an increased length of time each day thereafter for two weeks. He is then allowed to walk, the distance being increased each day, always avoiding even slight fatigue. Until the end of the sixth week or so the patient should lie down after each feeding. The length of time before he can attend to his usual affairs is at least two months;

the length of time before diet may be abolished varies from six months to a year. Bastedo says that the Lenz and von Leube diets should be forgotten. The principles governing the diet are, first, meals should be small, and second, they should be frequent. Food should be given every hour, if possible, during the waking hours to satisfy the caloric need, and to prevent accumulation of unsatisfied acid. Food should be bland, non-irritant, and arranged to combat hyperacidity or hypersecretion and hypersensitiveness of the stomach, even though high acidity is not always present.

The following is the feeding schedule as outlined by this author:

First day.—Peptonized milk, three ounces every one or two hours from 7 a. m. to 9 p. m. and once in night if patient is awake. Serve hot or cold, but not ice cold.

Second day.—The same, but four ounces every one or two hours.

Third day.—One egg in each quart; four ounces every one or two hours.

Fourth day.—The same; five ounces every one or two hours.

Fifth day.—Two eggs in each quart; five ounces every one or two hours.

Sixth day.—Three eggs in each quart; five ounces every one or two hours.

Seventh day.—The same; six ounces every one or two hours.

Eighth day.—Plain milk; three eggs in each quart; six ounces every one or two hours.

Ninth day.—The same, but for second feeding give saucer (five ounces) of oatmeal gruel or white cereal (arrowroot, cream of wheat, farina, hominy, rice) with cream or milk and sugar.

Tenth day.—The same, but for one evening feeding a saucer of junket, custard or farina with cream or milk and sugar.

Eleventh day.—The same, but at 1 o'clock, milk toast made with one full slice of toast, four ounces of hot milk, and one ounce of cream.

Twelfth day.—The same, but with two slices of toast with hot milk and cream. Make next feeding two hours later.

Thirteenth day.—The same, but for evening meal one coddled egg, one slice of toast and butter, and junket, custard, or farina with cream or milk. One glass of milk or water to drink.

Fourteenth to eighteenth day.—7 a. m.: Cereal as above, one poached or coddled egg, one slice of toast and butter, one glass of milk. 9 a. m.: One glass of milk and egg, or equal parts of milk and cream. 11 a. m.: Same. 1 p. m.: Minced chicken, creamed sweetbread or brain, or scraped cooked beef, one small baked potato with butter, one slice of bread and butter, milk or water to drink. 3 p. m.: One glass of milk and egg, or equal parts of milk and cream. 5 p. m.: Same. 7 p. m.: One soft

poached egg on toast, or soft boiled egg with toast, and custard, farina, blanc mange, junket, plain rice pudding or boiled rice with cream or milk and sugar. 9 p. m.: One glass of milk, or milk and egg with two plain crackers.

Nineteenth to twenty-eighth days.—Breakfast: Cereal as above, two eggs, toast, a glass of milk or cup of cocoa made with milk. 11 a. m.: A glass of milk and egg, or milk and cream.

Dinner: 1, Thickened, strained soup or purée, not made from meat stock, of potato, peas, beans, asparagus, corn, celery. 2, Chicken, lamb chop, beefsteak, creamed sweetbread, brain or stewed tripe. 3, Baked potato, creamed macaroni or spaghetti, rice, strained squash or carrots, asparagus tips. 4, Bread, toast or zweiback with butter. 5, Lettuce with olive oil and salt. 6, Milk or water to drink. 4 p. m.: A glass of milk and egg, or milk and cream.

Supper: One egg, toast or bread with butter, and a dessert—custard, jelly, farina, cornstarch, junket, vanilla ice cream, milk and cereal puddings, tapioca. 9 p. m.: A glass of milk, or milk and cream with crackers.

Fifth week and thereafter.—Hyperacidity diet.

Medical treatment consists of drugs to combat hyperacidity and hypersensitiveness with pylorospasm and measures to avoid intestinal stasis. For example, at the outset one might use sodium bicarbonate, half a level teaspoonful in half a glass of water, between feedings, from four to eight times a day. That this sets free gas when in contact with acid has not proved clinically to be a bar to its use. The milk of magnesia, one-half to one ounce with water, two ounces at bedtime, or magnesium oxide, 10 grains mixed with sodium bicarbonate are given during the day. Bismuth subcarbonate, 30 grains, with a little water may be given three or four times a day. This drug is not astringent, but is demulcent or protective. It may be given every two hours in 10-grain doses, alternating with sodium bicarbonate or mixed with it. A soap-suds enema daily is needed.

With duodenal ulcer without obstruction the intermittent character of the attacks makes the patient seem to be cured when he is not. Hence, freedom from pain and discomfort obtained by proper treatment, does not, of necessity mean a cure until time proves it to be permanent.

Medical Treatment of Gastric and Duodenal Ulcers. An article on this subject by Searle Harris,⁸ of Birming-

(8) Southern Med. Jour., November, 1916.

ham, is chiefly a reply to the statement of Moynihan that ulcer of the stomach or duodenum is amenable to surgery only. Harris considers the majority of such cases curable by medical treatment.

"The pessimistic viewpoint of surgeons regarding the curability of gastric and duodenal ulcer comes from the fact that they see only the advanced cases, and they have referred to them for operation the patients in whom there are complications; while the physician usually treats and cures the mild and uncomplicated cases."

Harris states that his own experience is in accord with that of other internists. In the past nine years in his private work he has treated more than 5,000 cases of digestive disease. He estimates that at least 10 per cent., or more than 500, had ulcer of the stomach or duodenum; and that at least three-fourths of them were cured—some of them under the most unfavorable circumstances. Probably 15 per cent. more were benefited, but had recurrences, and about fifty individuals were operated on. Hemorrhages occurred in probably twenty-five cases (fatal in only one), perforation in two, and in three the transition from ulcer to carcinoma was observed.

A history which indicated previous ulcer was obtained from a number of patients who were found to have cancer of the stomach, but in the majority of cases of gastric cancer no such history could be elicited. Therefore, in the author's experience, which, he says, is not different from that of others engaged in the same line of work, the serious complications of gastric and duodenal ulcer have been infrequent and the results from the dietetic and medical treatment so favorable that he believes this method should always be faithfully tried before surgery is considered.

In discussing active treatment Harris says: "The diet is of greatest importance and should be carried out thoroughly and systematically. A modification of the Lenhartz method has given me most satisfactory results over a period of nine years. It is based upon the physiologic principles of giving frequent feedings of small quantities of concentrated food to combine with the hydrochloric acid, without overdistention of the stomach,

yet of sufficient food value to build up the patient and thereby promote healing of the ulcer."

The following outline of diet is quoted:

MODIFIED LENHARTZ ULCER DIET.

First day.—1 egg, $1\frac{1}{2}$ $\frac{1}{2}$ cream, 4 $\frac{1}{2}$ milk. Mix and give $\frac{1}{2}$ $\frac{1}{2}$ every hour from 7 a. m. to 7 p. m. Total calories approximate 300.

Second day.—2 eggs, 3 $\frac{1}{2}$ cream, 8 $\frac{1}{2}$ milk. Mix and give 1 $\frac{1}{2}$ every hour from 7 a. m. to 7 p. m. Total calories approximate 600.

Third day.—3 eggs, $4\frac{1}{2}$ $\frac{1}{2}$ cream, 12 $\frac{1}{2}$ milk. Mix and give $1\frac{1}{2}$ $\frac{1}{2}$ every hour from 7 a. m. to 7 p. m. Total calories approximate 900.

Fourth day.—4 eggs, 6 $\frac{1}{2}$ cream, 16 $\frac{1}{2}$ milk. Mix and give 2 $\frac{1}{2}$ every hour from 7 a. m. to 7 p. m. Total calories approximate 1,200.

Fifth day.—5 eggs, $7\frac{1}{2}$ $\frac{1}{2}$ cream, 20 $\frac{1}{2}$ milk. Mix and give $2\frac{1}{2}$ $\frac{1}{2}$ every hour from 7 a. m. to 7 p. m. Total calories approximate 1,500.

Sixth day.—6 eggs, 9 $\frac{1}{2}$ cream, 24 $\frac{1}{2}$ milk. Mix and give 3 $\frac{1}{2}$ every hour from 7 a. m. to 7 p. m. Total calories approximate 1,800.

Seventh to tenth day.—6 eggs, 6 $\frac{1}{2}$ cream, 20 $\frac{1}{2}$ milk. Mix and give 3 $\frac{1}{2}$ at 8, 9, 10, 11, 12 a. m. and 2, 3, 4, 5, 6 p. m., and at 7 a. m. and 7 p. m. give two tablespoonsful strained oatmeal, 2 $\frac{1}{2}$ cream, level teaspoonful sugar and 1 soft boiled egg; at 1 p. m. 1 rounded tablespoonful scraped beef, lightly broiled, 1 heaping tablespoonful of rice and 3 $\frac{1}{2}$ milk. Total calories approximate 2,100.

Eleventh to fourteenth day.—Breakfast, at 7 a. m., and supper, 7 p. m., 2 soft boiled eggs, 1 slice of toast, 1 pat butter, 3 tablespoonsful strained oatmeal or cream of wheat, 3 $\frac{1}{2}$ cream, teaspoonful sugar. Dinner, at 1 p. m., 2 tablespoonsful scraped beef or minced breast of chicken, 2 slices dry toast, 2 heaping tablespoonsful of rice, butter and 2 tablespoonsful ice cream, 1 egg, 1 $\frac{1}{2}$ cream and 3 $\frac{1}{2}$ milk at 9 and 11 a. m. and 3 and 5 p. m. Total calories, 2,800.

Fifteenth to twenty-first day.—Same as from eleventh to fourteenth days except that the amount of cereal, cream and chicken or beef may be increased, baked Irish potato may be substituted for rice, and gelatine or boiled custard for ice cream. One egg, 1 $\frac{1}{2}$ cream and 4 $\frac{1}{2}$ milk should be given at 10 a. m. and 4 p. m. Total calories approximate 3,000.

From the third to sixth week.—The diet should be the same as in the third week except that strained orange juice may be given for breakfast and purées of peas, beans and potatoes may be given for dinner. Soft green vegetables mashed through cloth or sieve may be added. Total calories approximate 3,500.

He makes the further statement:

"In treating gastric and duodenal ulcers either medically or surgically it should be remembered that it is a secondary condition with which we are dealing, and one which is likely to return unless the underlying causes are sought for and removed. Focal infections in the teeth, tonsils, gall-bladder, appendix, or in any part of the body may be the exciting cause; but a localized area in the stomach must be the *locus minoris resistentiae*, and there are also predisposing causes to be sought for. Careful questioning of ulcer patients will usually bring out a history of gross errors in diet or in habits of living; and they are the same as those we find in patients suffering from hyperchlorhydria, which is usually seen in ulcer, and which nearly always precedes it. Rapid eating, insufficient mastication, over-eating, the ingestion of coarse foods, hot drinks, alcohol, coffee, tea, coca-cola and other caffeine beverages, the excessive use of tobacco, over-work, worry, grief, fear or other cause of functional hyperchlorhydria must be looked after."

Perforation of Gastric Ulcer. The perforation of a gastric ulcer occurring in the sac of a large congenital diaphragmatic hernia is described by Lennox Gordon.*

The patient, a man 56 years old, entered the hospital in a critical condition, presented evidence of peritoneal infection and physical signs in the chest as indicated in the accompanying diagram (Fig. 14). The symptoms and changes found were perplexing and a definite diagnosis was not made before the patient died. At autopsy the diaphragmatic hernia was found as indicated in Figure 15.

"The ring of the hernial sac was situated on the right anterior portion of the central tendon of the diaphragm in front of the liver and measured 4 inches in diameter. The margin was firm and tendinous with muscular fibers of the diaphragm blending with the tendinous ring anteriorly. The peritoneum became continuous with the serous membrane lining the sac."

"Laterally the sac extended to the costal wall, posteriorly to the vertebral column, except to the level of the seventh rib, above which the small rudimentary lung was situated. There was no lung between the sac and

(9) Brit. Med. Jour., Aug. 19, 1916.

the antero-lateral aspect of the chest. The contents of the sac were: (1) Most of the omentum, (2) the pyloric half of a largely dilated stomach, (3) the first part and the upper portion of the second part of the duodenum, (4) the right half of the transverse colon starting from

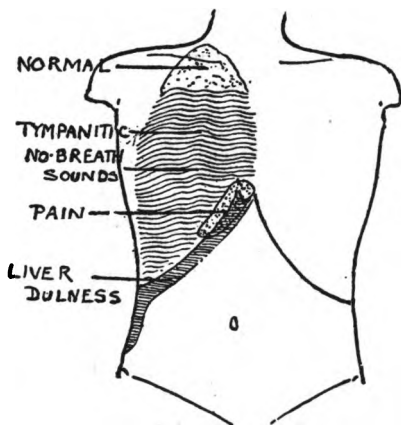


Fig. 14.

the hepatic flexure, and (5) portions of the small intestine (the exact length was not measured). All these organs were tightly packed into the sac and very firmly held at the ring. The parts within the sac were much congested, and showed that a certain degree of strangulation was present. It was only with a certain amount of force that the contents could be withdrawn from the sac. On the stomach being pulled down a perforation was found situated on the anterior wall 1 inch from the pylorus and therefore lying within the sac. The perforation was due to a rupture of a gastric ulcer having all the characteristics of that lesion, and not of ulceration the result of acute strangulation. It was apparently of recent formation. The hernial sac contained pus, the inflammation of the peritoneum having evidently started within the sac and spread to the general peritoneal cavity."

Gordon states that few reported cases of congenital

diaphragmatic hernia have been diagnosed during life. The signs and symptoms which would make one suspect that a diaphragmatic hernia was present are:

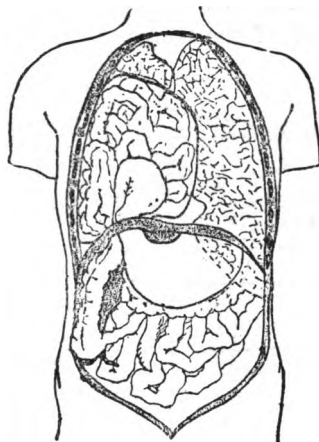


Fig. 15.

Restricted respiratory movement on one side of the thorax.

A tympanitic note on percussion with breath sounds limited in some parts of the thorax. If the bowels which occupy the hernial sac contain contents, then no tympanitic note may be obtained.

The heart is usually displaced, the displacement, of course, depending on the relationship of the heart to the ring of the hernia.

Signs of intestinal obstruction if strangulation of the hernia occurs.

Borborygmi may be heard on auscultating the tympanitic ring.

The most certain sign is that obtained from the *x-ray* after a bismuth meal. The bismuth will show the position of the bowel above the level of the diaphragm.

Treatment of Gastric Hyperacidity and Ulcer. The restriction of carbohydrates in the medical treatment of these conditions is discussed by Willard J. Stone¹ of Toledo. He says that gastric hyperacidity forms a very

(1) Jour. Amer. Med. Ass'n., Sept. 30, 1916.

considerable part of the symptoms of dyspepsia which the physician is called on to treat. It may exist (1) as part of the syndrome associated with prolapsed viscera and the attendant neurasthenic state coupled with a faulty dietary; or (2) as a result of reflex disturbance from some neighboring abdominal organ, such as the gall-bladder or appendix, or (3) as a result of faulty habits of mastication and the choice of appropriate food.

As has been mentioned in these books² before, this author places considerable stress on the relation between the increased consumption of carbohydrates and incidence of digestive disturbances. Figures have been compiled to show the great increase in the use of sugars in the different great nations of the world during the past thirty to forty years.

Clinically, he says, patients with hyperacidity, delayed motility and ulcer do better when their intake of carbohydrate foods is lessened. Deeks called attention to this in 1912. Although Stone does not subscribe to all the restrictions imposed by Deeks, he is convinced that excess of carbohydrates is a common dietetic error with such patients. He is also convinced that restriction generally to those articles of food which do not contain more than from 10 to 15 per cent. carbohydrates, with small additions of food which contain more than 20 per cent., such as bread and potato, together with sufficient alkali to limit the secretion of hydrochloric acid, has given better results than heretofore obtained. The following general diet list in hyperacidity has been found useful by Stone, though any articles may be omitted if necessary in given case.

Proteins and Fats.—Soft boiled or poached eggs, omelette, broiled or baked fish, bacon, chicken, oyster or clam broth, custard (use slight amount of sugar), butter, milk and cream, cream cheese, olive oil, tea.

Five Per Cent. Carbohydrates (Fodder-Vegetables and Fruits).—Asparagus, cauliflower, water cress, spinach, egg-plant, lettuce, beet or dandelion greens, string beans, olives, grape fruit pulp.

Ten Per Cent. Carbohydrates (Fodder-Vegetables, Fruits and Nuts).—Onions (boiled), squash, turnips, carrots, beets, lemon juice (one teaspoonful with one ounce olive oil twice daily as

(2) A previous article on the same subject by this author was abstracted in Practical Medicine Series, 1916, Vol. VI, p. 200.

salad dressing), orange juice and pulp, peaches, watermelon, cantaloupe or musk melon, hickory nuts, filberts.

Fifteen Per Cent. Carbohydrates (Fodder-Vegetables, Fruits and Nuts).—Green peas, parsnips, canned Lima beans, baked apple (pulp), pears, pecans, almonds, English walnuts.

The patient may take daily in addition, one potato, three slices of toast, one portion breakfast cereal or rice, purée of pea, corn ("Kornlet") or spinach.

Avoid excess sugar in above foods, candy, syrups, condiment sauces, pickles, green corn, tomato, cornstarch, macaroni, spaghetti, bread, crackers, cocoa, chocolate, coffee and vinegar.

In discussing the treatment of gastric ulcer the author states that it is necessary to secure absolute rest, usually in the hospital. Patients treated at home are usually unable to secure the rest and nursing coöperation necessary to the best results. In other words, they, as a rule can not be made while at home to attend strictly enough to the business of getting well. Although the details of the ulcer diet here given differ somewhat from the plans advocated by Lenhartz and by Sippy, the essentials are the same in so far as the attempt is made to control the supersecretion, to limit the secretion of hydrochloric acid and by frequent feedings and sufficiently large doses of the alkalies to prevent continuous local irritation of the ulcer area. This plan has been used with slight modifications since 1913 with good results in prepyloric, pyloric and duodenal ulcers.

Remarks on Treatment.—Neutral sodium citrate, 3 grains to each ounce of milk, may be given to prevent curd formation in the stomach.

Give from $\frac{1}{4}$ to 1 teaspoonful of alkaline powder (usually magnesium oxid 5, bismuth subcarbonate 5, sodium bicarbonate 20) after each feeding at 6 a. m. and 10 p. m.

The albumin water contains white of one egg flavored with orange or lemon juice, with no sugar.

If a taste of the milk remains in the mouth, use a weak borax mouth wash after each milk feeding.

If patient has been starved, give proctoclysis daily, by drop method, of 1 quart tap water containing 1 ounce dextrose.

TABLE 2.—ULCER FEEDING SCHEDULE.

Day.	Diet and Frequency.	—Time.—	
		A. M.	P. M.
1st	Milk, 2 oz., every 2 hrs.....	6	8
	Albumin water, 3 oz., every 2 hrs....	7	9
2d	Milk, 2 oz., cream, 1 oz., every 2 hrs..	6	8
	Albumin water, 3 oz., every 2 hrs.....	7	9

3d	Milk and cream as above, every 2 hrs.	6	8
	Albumin water, as above, every 2 hrs.	7	9
	One soft boiled egg, with feeding at..	7	7
4th	Milk and cream as above.....	6	8
	Albumin water as above.....	7	9
	One egg as above, with feeding at.....	7	7
	Soft, well cooked cereal, 3 oz., with feeding at	8	2
5th	Milk and cream as above.....	6	8
	Albumin water as above.....	7	9
	One egg as above, with feeding at....	7	1 and 7
	Cereal as above, with feeding at.....	8	2
	Purée, 3 oz., with feeding at.....	12 M.	6
6th	Milk and cream as above.....	6	8
	Albumin water as above.....	7	9
	One egg with 2 slices bacon, with feeding at	7	1 and 7
	Cereal as above, with feeding at.....	8	2 and 8
7th	Purée as above, with feeding at.....	12 M.	6
	Repeat above and 3 oz. broth, with feeding at	10	4
8th	Same as seventh and broth, with feeding at	10	4 and 10
9th to 14th	Same as eighth and $\frac{1}{2}$ slice toast with three feedings. Custard, 3 oz., may be substituted for one or two milk or albumin water feedings if desired.		

Butter may be added to cereal or egg if desired.

Avoid much sugar in preparation of custard.

Purée refers to pea, spinach or corn ("Kornlet").

Cereals refers to Cream of Wheat, Ralston's, boiled rice or Farina (measured after cooking).

Broth refers to chicken, oyster or clam.

Bacon should be fried crisp.

If retention of food exists lavage stomach one hour after last feeding at night.

Take weight of patient every alternate day.

Conditions which require surgery are discussed to some extent. Concerning the short-loop, posterior gastro-enterostomy as a form of treatment of gastric ulcer, the opinion is ventured that the operation would be far less popular if it were generally realized that by medical means the same results might be secured. This refers as well to the so-called obstructive types, in which, under the management here emphasized, the pyloric opening has increased as the spasm decreased. In the past it is safe to say that the operation of gastro-enterostomy has been frequently performed without adequate prior trial of dietetic and medical measures founded on principles

now well established. From the viewpoint of the physiologic principles involved, should operative means be indicated, excision of the ulcer and pyloroplasty has more to commend it and will probably in the future be the method of choice.

DISEASES OF THE INTESTINES.

Experimental Appendicitis. In a forty-page article with numerous photo-micrographs and several large tables of detailed observation, J. W. McMeans,³ of New York, gives an account of experimental appendicitis. This work comes from Cornell University, Surgical Division, and the Pathological Department of Bellevue Hospital.

In view of the widespread lesions observed in human bacteriemia, and with a desire to obtain more direct information on this subject, it was decided to study the effects on rabbits of the intravenous injection of micro-organisms derived from several sources.

Material for this work was obtained from appendices, from the tonsils of patients having appendicitis, from several pairs of tonsils and adenoid tissue removed in the children's clinic, from tonsils of fracture patients, otherwise apparently healthy, from pus of an infected hand. Among the appendices there were included two normal, two acutely ulcerated, three acute gangrenous, two with concretion and perforation, three with chronic infection, peritoneal fluid in one case of appendicitis, and pus from an abscess in the abdominal incision following operation for acute gangrenous appendicitis.

From the author's review of the literature it is evident that for a long time there has been recognized an apparent relationship between angina and appendicitis, with the result that several investigators have endeavored to prove that appendicitis occurs from hematogenous infection from the tonsil. Apolant saw three cases of appendicitis in conjunction with angina and thought that the organism entered the tonsil, and from there sought the *locus minoris resistentiae*. The controversy between those supporting the hematogenous

(3) Archiv. Int. Med., May, 1915.

theory and those of the opposition in favor of the enterogenous origin of appendicitis has waged fervently without a final decision.

The medium used for growing bacteria for this work was dextrose serum, used in 150 c.c. amounts, in Erlenmeyer flasks. In 125 rabbits injected intravenously with a variety of organism cultured by this method, gross hemorrhages were noted in the appendix sixty-two times.

If appendicitis is a local manifestation of a general infection due to a special organism, it should be possible, says McMeans, to demonstrate the organism in the blood at some time during the course of the disease. Until this fact has been definitely established for appendicitis, not including the pyemic type of the disease, one can little hope conclusively to prove that a particular organism is at fault. Kontzenberg, in a study of the opsonic index of appendix patients, found their serums acted equally well for a streptococci, staphylococci, and *B. coli*.

Further, the fact that a variety of different organisms have been associated with changes in rabbit's appendices, tends to indicate that a special organism has not yet been found. The production of appendicitis in animals by the intravenous injection of large doses of vigorous bacteria, can not be considered as an indication that these organisms attack the human appendix by way of the blood. Even in the most extreme cases in which the blood is overwhelmed with bacteria, the appendix is only occasionally involved. The condition produced in the appendix of the rabbit is primarily intramural, and is the analogy of a particular type of human appendicitis observed in pyemia. It can not be compared with the common type of appendicitis as described by Aschoff. At present, all authors are agreed that infection is requisite in the production of appendicitis. However, the widely divergent theories which have been advanced, including stasis, the hematogenous, alimentary theories, the idea of the similarity between tonsils and the appendix, and lastly the effect of fecal concretions, indicate that the appendix is the subject of many insults. Further, the comparison of the lesions which occur in

the appendices of animals in this type of experiment with human appendicitis should be made with extreme caution, as the disease in the animal is produced by very vigorous methods, and never assumes the character of the disease as it is observed in man. McMeans thinks that protest must be made against the idea that any organism possesses a peculiar affinity for any given organ, when the same organism shows a capacity for the invasion of other organs in a very appreciable proportion of experiments.

As the result of the present study of literature and experimental work, little evidence is found to support the belief that appendicitis in the human subject is ordinarily caused by a blood infection.

Melanotic Sarcoma of the Small Intestine. This interesting case is reported by E. A. Van der Veer and E. Kellert⁵ of Albany, N. Y.

The first symptom noted was a gradually increasing constipation which was only relieved by powerful cathartics. The second symptom was pain in the left upper quadrant of the abdomen which became progressively worse. These were practically the only symptoms. Finally, acute obstruction occurred; the tumor caused intussusception so severe as to cause the attending physician to decide on operation.

A tumor was found which filled the entire lumen of the ileum. Six inches of intestine were resected and an end-to-end anastomosis made. Recovery from the operation was tedious but uneventful. Six months later there was metastasis of the growth to the lungs to which the patient succumbed.

Syphilis of the Duodenum. In the case reported, J. L. Mortimer¹ made a diagnosis of syphilis of the duodenum for the following reasons:

1. History of onset one year after marriage, the birth of a syphilitic child; husband died of paresis. Both Wassermann reactions and symptoms cleared up previously under antisyphilitic therapy.

2. Presence of a hard irregular mass in the right hypochondrium.

(4) New York State Jour. Med., July, 1917.

(1) Amer. Jour. Syphilis, April, 1917.

3. Roentgen signs which show decisive evidence of postpyloric pathology.

4. Positive Wassermann reaction.

5. The marked improvement under antisyphilitic therapy, the patient stating that she was entirely free of abdominal pain and tenderness.

6. The diminution in the size of the tumor.

Infarctions of the Intestines. A comparison of the necropsy findings with the clinical course in cases of obstruction of a mesenteric artery or mesenteric vein in four men from 24 to 72 years old is made by A. Berntsen.² In one case there had been contusion of the abdomen three weeks before. In another, there was a history of abdominal pains at times for years and also of recent pulmonary trouble. The microscope showed phlebitis and thrombosis in the small mesenteric veins. In the younger man the thrombosis was secondary to incarcerated inguinal hernia which had been reducible for fifteen years. The prognosis is bad, but operative treatment is always indicated. The onset of trouble may resemble that of ileus. With embolism it is sudden and acute, the thrombosis being more insidious. Bloody diarrhea is almost the only differentiating symptom; this may occur with invagination, but the latter is encountered almost exclusively in children. There is bloody diarrhea in only a small proportion of cases of intestinal infarction.

Intestinal Eosinophilia. The occurrence of eosinophilic cells or Charcot-Leyden crystals in the mucus of stools has been occasionally reported almost ever since Ehrlich first described the eosinophile in 1879. They have been found with greatest frequency in cases of parasitic disease, especially amebiasis and hook-worm disease, and in the latter condition the finding has been reported to be an almost constant one. A single instance of this kind is now reported by George D. Barnett³ of San Francisco.

His patient was an Italian cook, 40 years old. The previous few months he had had an occasional attack of diarrhea alternating with constipation. During these

(2) Hospitalsdende, Aug. 30, 1916.

(3) Archiv. Int. Med., May 15, 1917.

attacks the bowels moved five or six times a day and he frequently noticed masses of mucus in his stools and at times blood. A differential account of smears taken from the circulation contained 47 per cent. of eosinophiles. Microscopically a very few ova of trichuris were found in a specimen of stool after an extensive search with special methods. Proctoscopic examination demonstrated in the rectum everywhere a glairy mucous pus and bright red blood.

This case is said to fall readily into the group of intestinal eosinophilia with definite proctoscopic findings, but differs from the type of eosinophilic proctitis reported by other observers, mainly in the marked blood eosinophilia and in the finding of trichuris ova in the stools. The author is not inclined to attach great importance to the finding of the trichuris ova.

In connection with the subject of intestinal eosinophilia, the statement of Schlect and Schwenker is referred to, in which it is said that the anaphylactic bowel in the dog shows an intense local eosinophilia. These experiments clearly suggest the possibility that both the local and blood eosinophilia in patients, such as the one whose case is reported here, may be due to the par-enteral digestion of protein by the patient, though we have no knowledge of the nature or portal of entry of such protein.

Autogenous Colon Vaccines in the Diagnosis and Treatment of Chronic Intestinal Toxemia. G. R. Satterlee⁴ of New York says that our modern conception of chronic toxemia is that of a diffuse toxemia of intestinal origin, the result of aberrant biochemical conditions, usually, but by no means always, bearing a measurable ratio to the delay in the onward passage of the intestinal contents.

The colon bacillus has its normal habitat in the large bowel, where it probably plays an important part in the end of digestion. Researches show that the colon bacilli elaborate materials which exert marked inhibitory influences on the putrefactive bacteria in the intestine, particularly the *Bacillus putrificus coli*, and in this way pre-

(4) Jour. Amer. Med. Ass'n., Dec. 9, 1916.

vent the origin of intestinal auto-intoxication. Carbohydrate oxidation and fat decomposition; fermentation, not putridity, are caused by the *B. coli* action. Under normal conditions it lives a saprophytic existence and is not only harmless but beneficial to the host. It is probably for this reason that results from sterilization of the intestinal tract have no lasting effect on the intestinal toxemia when the toxemia is thoroughly rooted in the system. When the colon is diseased, however, the colon bacillus is distinctly harmful, either in the walls of the colon or when lodged in other parts of the body, as the peritoneum, genito-urinary or respiratory tract, etc. It is then capable of becoming pyogenic and its intracellular poison is set free and can then act on the body of the host.

Satterlee quotes Vaughan, who says that the bacterial cell must die to liberate the poison; Deaver, who states that the *B. coli* isolated from the intestine in case of disease of that structure is more virulent than that from the normal intestine; and Adami, who says that under ordinary circumstances the *B. coli* is incapable of forming ectotoxins, but when the intestinal mucosa is affected by traumatism from within or without, the *B. coli* may wander and cause inflammation and thus liberate toxins.

It is necessary under these circumstances that bacteriolysis take place through a breaking-down and liberating of the resulting split products.

It is Satterlee's belief that a severe gastro-enteritis or a severe acute disturbance of the gastro-enteric functions is often the starting point and causative factor for the biochemical changes in the intestinal epithelia and the *B. coli* that occur later in the disease. The condition of chronic intestinal toxemia is not altogether unlike that of intestinal obstruction, in which the intestinal epithelia probably play an important part, as shown by J. W. Draper's⁵ experiments of causing the symptoms in animals by feeding heterologous jejunal and ileac epithelial cells. Murphy and Brooks also caused symptoms of intestinal obstruction and death in animals by injecting intravenously epithelial cells. They consider the symptoms and cause of death to be due to absorption of a

(5) Page 225, this volume.

toxin which is formed by bacterial growth and does not pass through a normal mucous membrane.

From the clinical study of his cases, Satterlee believes that after an intestinal toxemia is once established, the effect on all the body cells may be of long duration and that it is not merely a local condition, but a general one. As examples of this, he cites the histories of two cases.

The author reviews the literature on the use of colon bacillus vaccines.

The finding of colon bacilli in the blood is not necessary for the diagnosis of infection by this organism; if we had to wait for that we might never make a diagnosis, because it is very infrequently found. What we have to contend with, says Satterlee, is not the number of organisms but their virulence, and the degree of resistance of the individual.

Satterlee gives his technique as follows:

The initial dose is from 10 to 25 million of the dead bacteria subcutaneously, depending on the amount of toxemia in the individual. This dose is repeated at intervals of every four to seven days. The dosage is gradually increased by 25 million each time until the maximum of 200 or 300 million bacteria is reached. Relief of symptoms is not usually obtained until three doses have been given. Occasionally quick response is seen and sometimes two months are necessary. In most uncomplicated cases three months of treatment gives permanent relief.

In those patients who have a relapse, quick response to vaccine injections is usually given. In very obstinate cases it may be necessary to continue the vaccine treatment for a year or more.

A reaction after the injection of the vaccine usually occurs. This consists of a local redness, the size of a fifty-cent piece, pain and swelling at the site. In a severe reaction this swelling spreads until the whole upper arm is involved. This local reaction begins in six to eight hours and lasts twenty-four to seventy-two hours. At the same time a general reaction takes place. A brief description of this is that there is an exaggeration of all the symptoms: headache, malaise, vertigo and occasionally nausea; a decided increase in the severity

of neuralgic or myalgic pains and of pain, soreness or discomfort in the abdomen, if these symptoms had been present. This reaction is followed by decided relief of all the previous toxic symptoms.

In markedly toxic cases if an active colon organism from the diseased part of the colon has been obtained, early reactions are severe. The reactions have usually been severe in most cases in which excessive doses, such as 300 to 1,000 million bacilli, have been administered.

In those cases in which no reaction is obtained the cause may be (a) attenuation of the organism from which the vaccine has been made; (b) previous immunization of the patient, as after prolonged dosage of vaccine; (c) mild degrees of toxemia, or (d) absence of colon bacillus toxemia in the body. In the last-stated cause the vaccine becomes of value in diagnosis.

In no case of profound intestinal toxemia, as yet, has there been a complete absence of reaction following the administration of the vaccine. The converse also holds good, that in no case in which a sharp local and general reaction has taken place would chronic intestinal toxemia be excluded.

Loose bowels and intestinal evacuation have occurred in quite a few instances, following the vaccine injections, and improvement continued.

The following classification for use of autogenous colon vaccines has been suggested by the author's success in the vaccine therapy: (1) mild chronic toxemias which do not respond to diet; (2) all severe chronic toxemias; (3) operative cases, (a) before and (b) after operation; (4) doubtful cases, as an aid to differential diagnosis.

It is essential to make a thorough study of every case, which includes a radiographic gastro-intestinal investigation. Symptomatology is important, but the physician should not take any patient's word or personal opinion about the state of his bowels. In numerous instances "absolutely regular bowels" are proved to have large residues.

Satterlee thinks it pretty certain that all patients with chronic intestinal toxemia have had constipation at some time and that this is a very strong etiologic factor, and also that the laxative habit does not cure, but rather

aggravates the toxemia. To prove this we find many "residual cecums," "sigmoids," etc., in patients who have regulated bowels by taking cathartics or laxatives weekly. But these patients have symptoms of toxemia, which are frequently not recognized. Nature often finds its own best relief, so the physician hears: "the osteopath has given me most help, but has not cured me."

On account of the predominance of nervous and mental symptoms, these people frequently consult the neurologist, who, if thoroughly up to date, should recognize the trouble and institute proper diagnosis and treatment. There are undoubtedly many cases of primary nervous system lesions in which the gastro-intestinal toxemia is secondary. There is every reason that these patients should have the proper care of the toxemia, even if it is a secondary complaint. The insane asylums claim their share of chronic intestinal toxemias. As examples, three of the patients under consideration in this paper had been declared insane and are now well. One patient, an old lady of 76, with the diagnosis of senile dementia, has had the mental symptoms cleared up for weeks at a time by means of dietetic measures and autogenous colon vaccines, which have had remarkable and lasting results.

The author analyzes sixty-four cases and the results from this vaccine therapy. In seventeen operation was an essential part of the treatment.

He concludes his article with the following summary:

The predominating factor in the symptomatology of chronic intestinal toxemia is the colon bacillus.

In diseased conditions of the colon, the colon bacillus may become very harmful to the human organism by forming and liberating toxins, thus causing a toxemia.

This toxemia gives a definite symptomatology called chronic intestinal toxemia.

Putrefactive organisms often play an important part in intestinal toxemias, but the lasting effects are due to the colon bacillus.

In the study and treatment of all long-standing or severe chronic intestinal toxemias, autogenous colon vaccines should be administered in proper dosage.

Autogenous colon vaccines are helpful in the diagnosis of chronic intestinal toxemia.

The method of action of the colon bacillus vaccine is probably an immunization and sensitization of the body cells.

Intestinal Auto-Intoxication. A clinical investigation of intestinal auto-intoxication, with special reference to the specificity of toxins, has been made by Thomas R. Brown⁶ of Baltimore. An account of three patients with eczema as a symptom of the condition under consideration is given. Tests were made by which it was determined that two of these patients were sensitive to milk, egg-white, horse serum, meat juice, and barley. The third patient gave no reaction indicating a sensitiveness of any degree to these proteins. In the first two instances a meat-free diet with no cereals brought about a rapid improvement leading to a permanent cure, while in the third case there were no effects from such management. The two patients whose condition was improved in this way were able later to add proteins to their diet gradually without the return of their former trouble.

Brown also refers to an instance of severe pruritus that was apparently due to sensitiveness to proteins. • On a low protein diet, practically meat-free, with milk entirely eliminated, and the administration of hydrochloric acid (in this patient there was also achylia gastrica), and attention to the chronic constipation that was of years standing, the pruritus gradually disappeared and acid was found in the stomach contents. Note is made of two other patients who suffered with chronic constipation, attacks of bilious headache, and achylia gastrica. These were markedly relieved by using a diet that was practically free from animal proteins, and the attacks, plus a definite temporary enlargement of the liver, could be brought on by feeding meat for a short period.

A woman, 27 years old, complained of chronic constipation of thirteen years' duration, and attacks of eye-ache and impaired vision for four years. She was found to have visceroptosis, a high degree of cecal stasis, chronic appendicitis, and chronic chorioiditis. Her stools

(6) Amer. Jour. Med. Sci., December, 1916.

were alkaline practically all the time and from them there were isolated anaërobic, Gram-negative diplococci, and a small anaërobic, Gram-negative bacillus. A low-protein diet was instituted, an appendicostomy operation done and colonic irrigations made through the new opening. Considerable improvement was brought about by these measures. The chorioidal attacks recurred at intervals, and the return could be predicted by the alkalinity of the stools and the presence in them of the anaërobic organisms referred to above.

In discussing this subject the author states that when toxic symptoms are spoken of debatable ground is entered upon, and yet certain of the symptoms met with in these cases are explicable only on this basis. What is the cause of these toxic symptoms? It is a toxin normally present or in excess? Has the protective mechanism become insufficient, possibly due to repeated mild anaphylactic reactions, or is there a tendency toward an overgrowth of certain bacteria, notably proteolytic anaërobes, and may immunity be brought about in time? Whether these toxins are derivatives of the amino-acids can not be said, but it is striking what slight changes in molecular constitution are necessary to convert the normal bases into products of great toxicity, and it is certainly possible that this may be brought about by the proteolytic intestinal bacteria. The work of Eppinger and Guttman in isolating two ptomains from the stool, one producing urticaria, the other asthma, is extremely suggestive in this connection. Whether these toxic anaërobes are always present in minimal amount, or whether they originate from external sources, such as tainted meat or pyorrheal pockets, has not been determined. That the poisons, produced by these bacteria or due to other causes, can not often be demonstrated is not so much a proof of their absence as of their extreme complexity, and of the minimal amounts in which they must be present in urine, blood, and stool. The mechanical and surgical conceptions of intestinal stasis are quite insufficient to explain the symptom-complex presented. Back of the mechanics of digestion lies a problem far more complicated, far more difficult to solve, the problem of congenital or acquired hypersensibility to certain

stimuli, the question of the overproduction of certain toxic substances, their chemical nature, and their possible specificity, and various questions involving more definitely physical factors, notably absorption and osmosis.

From his own experience the author concludes that in the intestine certain substances are produced which in some instances are possessed of specific action associated with a hypersensitiveness to certain proteins not in themselves toxic but possibly capable of producing a reaction because of an acquired hypersensibility, and that therapeutically a marked improvement in symptoms and even a complete cure may be brought about by the elimination of these substances from the dietary. It is also suggested by a study of these cases that by giving these foods in gradually increasing amounts a marked increase in resistance may be produced. That in certain cases at least the symptoms are better explained on the basis of a bacterial infection of intestinal origin rather than upon that of a toxemia, and that in various cutaneous lesions, testing the cutaneous sensibility by intradermal injection of various proteins is of real value in determining whether or not the condition may be due to certain toxic bases of intestinal origin derived from the decomposition of certain protein foods. These reactions are apparently specific in character, that is, are only found to be present when the toxins produced have a specific effect upon the skin, and therefore these tests of cutaneous hypersensitiveness to various proteins probably can not be used as criteria of other conditions best interpreted as protein intoxications with manifestations elsewhere than in the skin.

Intestinal Obstruction. According to J. W. Draper,⁷ of New York, intestinal obstruction is no longer an abstruse laboratory study but a many-sided problem of quite as great interest to the abdominal surgeon as to the surgical physiologist.

He cites in detail experiments made to determine the effect of feeding jejunal and ileac mucosa to duodenally obstructed dogs; the duration of life in esophageal and gastric obstruction; the effects of introducing into the peritoneal cavity the scraped epithelium of obstructed

(7) Jour. Amer. Med. Ass'n., Oct. 7, 1916.

and non-obstructed dogs; the isolation of intestinal doubly occluded loop with reconstruction of alimentary canal and curettage of epithelium having cells within the loop; and production of Thiry-Vella fistulas, a single occluded duodenal loop, drained externally, reconstruction of the canal. The author states that determination of the origin of the toxemia in dogs is important in studying the etiology of constipation in man. He reaches the following conclusions:

The cause of death in intestinal obstruction is still unknown, but all recent studies point to aberrant activity of the duodenal and probably pancreatic cells. The old hypothesis that the toxin is of bacterial or food-decomposition origin may be looked on as discarded. Dehydration is of no greater importance in this than in other toxemias.

There is an important ratio between the toxicity of the intestinal epithelium and its digestive power.

The intricate syndrome autotoxemia occurring in man will be better understood when we know the cause of death in duodenally obstructed dogs.

Discussion of Intestinal Stasis. In a discussion of this subject, G. R. Satterlee,⁸ of New York, defines chronic intestinal stasis as a diffuse intoxication of unknown origin, the result of aberrant biochemical conditions, usually, but by no means always, bearing a measurable ratio to the delay in the onward passage of the intestinal contents, as visualized by the Roentgen-ray.

He says that very little is known regarding the etiology of toxemia, but it has been supposed that constipation was the usual exciting cause. Whether the toxemia is traceable to bacterial causes or to disturbance in the internal secretions of the gut itself is unproved, but of the two the bacterial hypothesis has rather more support than the biochemical, from therapeutic results. Nevertheless, though many mild cases respond to protein-free diet, graver ones usually will not, and these in turn may or may not react favorably to autogenous colonic vaccines. One thing is said to be certain from the study of this series, namely, that congenital or ac-

(8) Amer. Jour. Med. Sci., November, 1916.

quired deformity of the gut is a strong predisposing factor.

Regarding the pathology, he thinks that observations to be of any value at all must be made on the fresh post-operative tissues rather than on dead-house material, the latter having led many observers into the gravest kind of errors on account of the rapidity of post-mortem changes.

Symptoms, he says, remain the dominant factors in establishing a diagnosis. Multitudes of sufferers from neuralgias, myalgias, neuritides, hemicranias, neurasthenias, amauroses, etc., are maltreated for the symptom rather than for the cause. And yet how little is known regarding the greater problem of the relation of subtle, yet powerful, toxemia to the more serious and better-defined lesions of the cardiovascular, central nervous, and genito-urinary systems, which some of the more advanced observers consider to be reflections of this fundamental bowel perversion.

Classification of these cases of intestinal toxemia, according to symptomatology, is too indefinite, so Satterlee has adopted one according to the location or locations of the lesion. Neoplasms and unusual obstructions are omitted.

(a) Gastric delay, due to gastric atony, water-trap stomach, and reflex causes.

(b) Duodeno-jejunal obstructions, so frequently looked on as evidence of intestinal toxemia and believed by Lane and Bloodgood to be mechanical.

(c) Ileocecal obstruction and non-obstructive ileac constipation.

(d) Chronic appendicitis.

(e) Cecal dilatation and constipation.

(f) Atonic constipation of the colon, especially of the transverse portion. (Here may also be grouped the dubious so-called spastic constipation.)

(g) Sigmoid constipation.

(h) Lesions of the rectal outlet.

(i) Combinations of these forms.

The autotoxic patient's chief complaint, as shown by Satterlee's tabulated study of 136 cases, is extremely variable. In fact, its variability and its apparent com-

plete separation from the intestinal canal are often its chief characteristics.

Constipation as a primary or secondary complaint appears in 114 cases, or 84 per cent.; diarrhea, in thirty-nine, or 30 per cent., of which number thirty gave a history of both diarrhea and constipation. In five the history was unreliable and in eight the bowel movements were normal. Colica mucosa occurred in fifty-nine, or 43 per cent. Flatus was present to a marked degree in 105, or 76 per cent. Loss of weight occurred in eighty, or 60 per cent. Mental symptoms varying from simple inefficiencies to melancholias, and epilepsies, deliria and stupors occurred in fifty-four, or 40 per cent. Nerve symptoms, neuralgias, etc., occurred in eighty-eight, or 65 per cent.

Enteroptosis was absent in only thirty, or 22 per cent. Gastric constipation, as determined by the six-hour bismuth meal, occurred in fifty-four cases, or 40 per cent.

Ileac constipation was present in three. "Residual cecum," as determined by remnants of bismuth barium in the cecum and the oral part of the ascending colon forty-eight hours after ingestion, was present in fifty-eight cases. Colonic delay of between forty-eight and seventy hours was found in thirteen cases.

A residue in the sigmoid of more than three days' duration was noted in forty-seven patients. Of the entire series, thirty-three, or 25 per cent., had had the appendix previously removed without lasting benefit to the chronic condition.

The author's views and observations upon colonic vaccines have been significant both in differential diagnosis and in therapy. The vaccine is prepared in the usual way from the prevailing type of colon bacillus, isolated from the patient's feces. The dosage is of very great importance, and injections should not be given when the bowel is loaded, else an unnecessarily severe action is apt to result. This in itself is an interesting and perhaps significant fact. The initial dose has been from 25 million to 50 million, continued at intervals of from four to seven days, and the maximum dose 300 million bacilli.

After some reference to a number of patients treated in this manner, Satterlee says that the general consensus

is that vaccines are useful for the cure of local infections, but they may also be of use in some general instances. If it is true that intestinal toxemia is due in some instances to the end-products of colon infection, and that the infection is localized to the intestinal tract, or its immediate neighborhood, immunization by means of vaccines would not be an irrational method, just as their usefulness has been recognized by some physicians in colon infections in the genito-urinary tract or elsewhere.

Chronic Intestinal Stasis. In a discussion of this condition and its medical treatment, William Van V. Hayes,⁹ of New York, mentions the following symptoms as common:

Headache, indigestion, bad taste, belching, burning, sour regurgitation, epigastric discomfort or pain. Sometimes there are nausea and vomiting—bilious attacks. Constipation is common, although the movements may be regular or even loose. Dizziness, depression, weakness and lack of endurance are frequent.

Common signs found by physical examination are: pale and sallow skin, out of proportion to any anemia present. Weight and strength are diminished and the extremities are cold. The tongue is flabby and indented. Ptosis of the stomach and intestines and an atonic gastric wall are found. The duodenum is dilated with gas, but readily empties by lifting the abdomen. The ileac coils often contain gas. The left ileac colon is frequently spastic. The ileocecal valve is found to be incompetent.

The *x*-ray, Hayes says, has proved itself invaluable in accurate diagnosis of abdominal conditions, including chronic intestinal stasis, and should be used, if possible, in every obscure case. It is helpful in showing the gastropnoia so often present, the dilatation of the duodenum, the ileac stasis, incompetence of the ileocecal valve, displacements and dilatations of the colon, and deformities or partial obstructions due to bands.

Concerning the frequency of stasis, it is probably safe to say that more than half of all cases with chronically disturbed digestion are suffering from some degree of chronic intestinal stasis, alone or with complications.

(9) Interstate Med. Jour., March, 1917.

The author quotes Lane, who says that there are three groups of cases for separate kinds of treatment. First, about 90 per cent. of the cases are suitable for medical treatment; second are cases requiring corrective surgery, freeing of bands, kinks, etc., and third are severe cases requiring a short-circuiting operation or colectomy.

Under medical treatment, support to the abdomen is recommended, and for this purpose a good belt or spring support is ordinarily most effective, though corsets answer very well in some cases. To raise and maintain in position the digestive viscera, particularly the intestines, is considered by Hayes a valuable step in the treatment. The patient should be taught to maintain correct poise of body, with chest forward, shoulders back and abdomen drawn in. Massage with the pressure so applied as to raise the ileal coils and propel the contents along the colon; special exercises given to strengthen the abdominal muscles, especially such as can be taken lying on the back; a glass of water taken an hour or more before meals and at bed time; liquid petrolatum (heavy and highly refined), from one-half to one ounce on rising and retiring, or one-half hour before meals are measures that the author considers often helpful.

Extract of cascara, 1 to 5 grains; compound licorice powder, $\frac{1}{2}$ to 1 dram; phenolphthalein, 1 to 2 grains, or agar-agar, with phenolphthalein, $\frac{1}{2}$ to 2 drams, p. c., or an occasional dose of calomel may be given if necessary.

Carlsbad sprudel salts, $\frac{1}{2}$ to 1 dram in half a glass of water on awakening, or a similar saline, a full hour or more before breakfast, may be desirable for limited periods.

Out-door life and systematic exercise—golf, tennis, horseback riding, automobiling, calisthenic and gymnastic drills, general massage, hydrotherapy or other measures should be encouraged, as may be indicated to improve as much as possible the nerve tone and muscular vigor of each patient.

The histories of a number of patients treated by the author are given in detail.

Treatment of Intestinal Stasis. The question of partial or total colectomy, and of short-circuiting the bowel,

is discussed by J. H. Kellogg.¹ He refers to the theory of Metchnikoff, who, it is said, announced about 1902 that the colon was a useless appendage and that the colon bacillus was the germ of old age. Soon after this, Lane began the practice of surgery of the bowel that has been so well known for years.

During the last ten years, Kellogg has performed colectomy on twenty patients; in four of these, who had already had short-circuiting operations, it was done for intestinal stasis.

These twenty cases have been selected from more than 40,000 cases which have been treated in the Battle Creek Sanitarium clinic during the last ten years, or less than one in 2,000. Most of these patients have been found to be suffering from intestinal stasis, but they were relieved by non-surgical means, or by simple restorative surgical procedures.

The non-surgical means which he has found most effective in relieving intestinal stasis are the following:

A low protein, bulky diet, consisting largely of fruits, fresh vegetables and whole grain preparations.

The free use of bran or agar-agar, or a combination of both, at every meal. From one-half ounce to an ounce of cellulose daily seems to be necessary to stimulate the bowels to normal activity.

The use at every meal of from half an ounce to an ounce and a half of liquid petrolatum. In some cases an emulsion of liquid petrolatum gives more satisfactory results, and the best results are often obtained from the use of petrolatum (which melts at the temperature of the body).

Abdominal massage and special exercises for developing the abdominal muscles.

In very obstinate cases the patient takes, three or four times a day, a couple of tablespoonfuls of bran and as much fruit as he can eat. Fresh and stewed tomatoes are found to be especially useful. Lettuce and celery may also be used freely. The patient is allowed to take fruit between meals or whenever he feels inclined to do so. For persons suffering from hyperacidity, non-acid fruits, like bananas, pears, white cherries and melons,

(1) Jour. Amer. Med. Ass'n., June 30, 1917.

are used. Occasionally it is found advantageous to make the diet consist wholly of green vegetables, raw and cooked, with bran or agar-agar. This regimen will usually clean off the tongue and get the bowels moving three or four times a day within four or five days. Occasionally the regimen must be continued for a week or ten days. When mechanical obstacles to bowel action, such as prolapse of the pelvic colon and adhesions or other obstructive lesions, are not present, this method will very rarely fail.

At first it is occasionally necessary to use an enema at 80° F. once a day. The patient should be required to go to stool on rising in the morning and after each meal.

In cases of colitis with a spastic condition of the descending and pelvic colon, the colon is treated by means of hot saline enemas, and afterward there is introduced into the colon, with the patient in the knee-chest position, several ounces of a liquid culture of *Bacillus bulgaricus* and *Bacillus bifidus*, to which is added a small amount of malt sugar and boiled starch, the purpose being to change the character of the bacteria growing in the colon and thus encourage the healing of the infected mucous surface.

In cases in which the lower colon has lost its normal sensibility, various stimulating applications are made, among the most useful of which is electricity applied to the upper part of the rectum or pelvic colon by a bipole electrode; very weak solution of hydrogen peroxide (0.25 per cent.); solution of citric acid (from 0.25 to 0.5 per cent.), and a mixture of equal parts of carbon dioxide and pure oxygen gas (from 200 to 500 cm.).

In cases in which the mucous membrane is atrophied as the result of chronic proctitis, it is found very advantageous to introduce into the lower colon at night 3 or 4 ounces of a preparation of petrolatum which melts at the temperature of the body. Such a preparation may be made by melting together equal parts of liquid petrolatum and paraffin.

The wet girdle worn at night and a variety of other hydiatic procedures have also been found highly useful by Kellogg in dealing with stubborn cases of constipation.

Chronic Constipation. In this article, T. E. H. Thaysen² discusses what he calls "*Ascendensobstipation*," the condition in which the feces sojourn an abnormally long time in the ascending colon and first part of the transverse colon. There may be excessive or deficient contractions of this part of the bowel. In thirteen of Thaysen's twenty-two cases of this ascending type of chronic constipation the stasis was restricted to the ascending colon, and the x-ray showed the atonic or spastic conditions responsible for the constipation. In the other cases the roentgenograms showed stasis of feces along the ascending colon and beyond. Adhesions may be responsible for stasis in the descending colon, but this seems to occur but rarely, the trouble here being of a functional nature in the majority of cases, either spasmodic contraction or atony or a combination of both. Nine of his twenty-three cases were of the spastic type, and even in the others there were occasionally symptoms suggesting spasmodic contraction. He calls attention to the fact that in six of the nine spastic cases the pains were either exclusively on the left side or much stronger there than on the right side. In only two were they restricted to the right side; in one case to the epigastrium. The tenderness likewise was most pronounced over the regions where the pains were felt most. This suggests, he says, that when there is spastic contraction in the ascending or transverse colon, there must be an accompanying spasm in the descending colon. Among the fourteen patients with constipation from atony, four had no pains in the colon region, six had pains in the right iliac fossa, two in the left and two on both sides. The roentgenograms show that the ascending colon is not dilated with this "ascending" constipation. It is liable to lead to the erroneous diagnosis of appendicitis, especially of "recurrent" appendicitis, while mucous colitis rarely entails appendicitis. Four of Thaysen's patients had a temperature somewhat above normal along with pains in the right iliac fossa, confirming the assumption of appendicitis. The disturbances in such cases persist after removal of the appendix, as this does not get rid of the cause. In short, Thaysen concludes, the discovery of

(2) Ugeskr. f. Læger, Dec. 14, 1916.

Ascendensobstipation should contra-indicate appendicectomy, even when everything seems to indicate chronic appendicitis.

Dietetic and Physical Treatment of Constipation. A. Borgbjærg³ directs attention to the fact that a number of factors may combine in producing constipation, such as reduction in the amount of fecal material, harder consistency, delayed passage through the intestines, infrequent desire to empty the bowels, and difficult defecation.

The x-ray shows that mechanical obstacles such as adhesions, excessive length of mesentery, enteroptosis, and movable cecum do not necessarily result in constipation. A more important factor in producing constipation is weakness of the muscles of defecation, but in the majority of cases, the author states, there is no mechanical cause which can be found. He has seen cases of severe constipation in vegetarians and he does not approve of a diet of exclusively coarse food for too long a time.

The length of time a patient may be allowed to go without a bowel movement is a matter to be decided for each individual patient. If the patient is carefully watched a week may be allowed to elapse, he thinks; he once allowed a patient to go thirteen days.

He never realized the importance of massage so long as it was applied in the patients' home and he saw the patients only at intervals. But since he has had his patients under constant supervision in his private clinic, he has become convinced of its value as an aid in treatment of constipation. He combines with gymnastic exercises, especially abdominal breathing exercises. When the constipation is the result of retention of the feces in the sigmoid flexure region or rectum or of inability to expel the feces arriving in the rectum, these measures and dieting do not seem to do much good. It is possible, he thinks, that benefit might be derived from internal massage of the rectum or vibration treatment or intrarectal faradization, as Boas advises. Borgbjærg has not had much experience with these measures but thinks them promising. He

(3) Ugeskr. f. Læger, February, 1917.

says further that the normal position for defecation is undoubtedly the squatting position. The depression, lassitude, etc., which are usually ascribed to auto-intoxication in case of constipation, he thinks are more often the result of worry over the supposed evil effects of the defective intestinal functioning.

Ulceration of Small Intestine. The main points of interest in the fatal case reported by D. R. Adams⁴ were: Death was due to peritonitis and perforation of the ileum following on multiple ulceration of the greater part of the small intestine. This ulcerative process had been going on for at least a week before death. The liver activities were to some extent in abeyance. The ulcers of the small intestine were associated with marked invasion of the alimentary tissue by an organism similar to the *Bacillus coli* which, as is well known, can produce indol from proteid and its derivatives. At one stage complete oxidation of the amino-acids into indigo and skatoxyl pigments took place in the body, causing indigo-uria. At a later stage this oxidation was less complete, and indican appeared in the urine.

INTESTINAL PARASITES.

Flagellate Diarrheas, Diagnosis and Treatment. Certain flagellate protozoa are frequently found in routine microscopic examinations of stools for entamebas and ova, and it has been determined that these flagellates, especially in individuals who have resided for a longer or shorter time in warm climates, produce gastro-intestinal disturbances resulting in diarrhea. In an account of some instances of this kind, Arthur F. Chace and Arthur N. Tasker⁵ describe three kinds of organisms found in some of their patients, recite the details of the disease, and the treatment used.

The three flagellates found as etiologic factors in diarrheas are shown in the accompanying illustration (Fig. 16), and are described here as in the original article:

(4) Glasgow Med. Jour., August, 1916.

(5) Jour. Amer. Med. Ass'n., May 26, 1917.

A. *Cercomonas hominis* Davaine.—In form this organism is irregularly round or pear-shaped, with the longer diameter measuring in the great majority of individuals from 8 to 10 microns. From the more rounded end there projects a single flagellum, which is

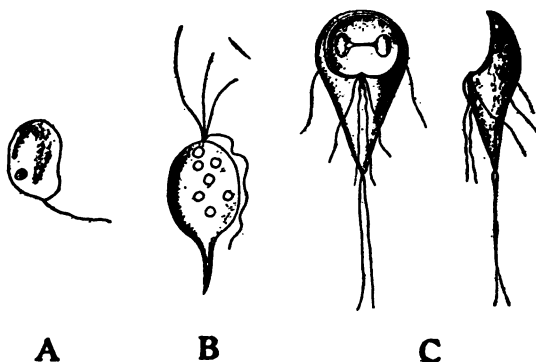


Fig. 16. Flagellates: A, *Cercomonas hominis* Davaine; B, *Trichomonas intestinalis*; C, *Lamblia intestinalis*.

in general nearly twice the length of the body. No undulating membrane is present. The nucleus is difficult to distinguish. In preparations of freshly voided intestinal contents examined microscopically the parasite is seen to be actively motile.

B. *Trichomonas intestinalis* Leuckart.—This protozoon is probably identical with *T. vaginalis* Donne, which was originally thought to occur only in vaginal mucus of an acid reaction and to be not transmissible to the human male. It is, like *C. hominis*, somewhat pear-shaped, but, unlike *C. hominis*, its smaller extremity is drawn out to a fairly definite and sharp point. It differs also from the previous organism in size, its longer diameter being from 15 to 25 microns, in the possession of an undulating membrane, and in showing at its rounded end three flagella instead of one. The nucleus is quite distinctly visible. In specimens of recently voided feces the parasite manifests active motility.

C. *Lamblia intestinalis* R. Blanch.—This third flagellate is also irregularly pear-shaped in outline. It is from 10 to 20 microns in length and its greatest breadth,

which is near the anterior rounded extremity, is about one-half of its length. The cytoplasm is seen to be finely granular and is surrounded by a thin cuticle, by means of which the organism is enabled to maintain a practically permanent form; that is to say, its outline varies by relatively slight changes only. The nucleus is of a dumb-bell shape and is situated in the anterior part of the body. On one side and near the anterior extremity is to be found a rounded excavation, which looks obliquely forward. This excavation is probably a sort of peristome and exercises the functions of a clinging organ. Four pairs of flagella serve to endow the parasite, as seen in freshly passed stools, with an active motility. The first pair of flagella arise from the anterior border of the excavation above described; the second and third pairs, from the posterior edge of the same organ; while the fourth pair take their origin from the posterior pointed extremity, or tail.

An accurate diagnosis of these conditions has as its only possible basis a microscopic examination of the intestinal contents. A drop of emulsified feces is placed on a warm slide, covered with a No. 1 cover glass, and examined under the high dry objective. The active movements of these organisms, which are entirely different in character from those of amebas, will quickly, easily and surely call attention to their presence. Specific determination can then be made by further study of individual specimens under the oil immersion objective, bearing in mind, of course, the morphologic characteristics hereinbefore described.

In view of the etiologic factors, it will without doubt be readily accepted that the ordinary methods of treatment which are employed in cases presenting similar symptoms, but which are of non-specific causation, will be of little avail if made use of in the flagellate diarrheas. As a matter of fact, bismuth and opium and all similar combinations of astringents and opiates are well-nigh useless in the therapeutics of these conditions. On the other hand, however, it is a fact which should not be lost sight of that merely putting these patients at rest in bed is often followed by a disappearance of the parasites and an improvement in the character of the fecal dis-

charges. This does not constitute a cure, for within a certain length of time after such a patient has resumed his normal activities he will almost surely suffer a relapse.

The best therapeutic measure available in the treatment of infection with any one of these parasites, the authors believe to be the administration, both by mouth and in the form of high enemas, of Merck's medicinal methylene-blue, the chemical name of which is methylthionine hydrochloride. It is essential that only the medicinally pure drug should be used, as the methylene-blue ordinarily employed in laboratory staining solutions contains traces of zinc. The patients in whom this treatment is instituted should be warned that during the process of elimination of the therapeutic agent the urine will be blue in color. It is the custom of the authors to give 2 grains every three hours by mouth and to administer at least once and preferably twice a day a high enema, which should be retained for fifteen minutes, consisting of 500 c.c. of an aqueous solution of the drug, the strength of which is to be between 1 to 500 and 1 to 200. It is said that methylene-blue seems to have much less of a specific action on trichomonas and lamblia than it exerts on cercomonas. On the other hand methylene-blue is, so far as these workers know, the only drug which manifests any appreciable effect at all on either trichomonas or lamblia. Ipecac and its alkaloids, if of any value whatever, certainly do not possess the same parasitocidal effect that they exhibit in their action on amebas.

The fact that these organisms are probably transmitted through the medium of drinking water and of fresh vegetables which are eaten uncooked after being previously fertilized with human excrement suggests the available methods of prophylaxis. All drinking water which is not entirely above suspicion of fecal contamination should be efficiently sterilized before use. The same of course applies to all water which is taken into the mouth in cleansing the teeth or for other purposes. Similarly, the use of vegetables, tubers, and fruits usually eaten uncooked which come from truck gardens where it is customary to use human fecal material as fertilizer should be discontinued, or if such articles

of food are used at all, they should be thoroughly cooked.

Treatment of Flagellate Infections of the Intestines. In this article, H. L. McNeil,⁹ of Galveston, Texas, describes the treatment used by him in these cases. It consists of direct irrigation of the duodenum with solutions toxic to the parasites but harmless to the patient.

He has used the following solution in numerous cases: Methylene blue (medicinally pure), 5 grains; quinine sulphate, 20 grains; hydrochloric acid (concentrated), 30 min.; distilled water sufficient to make one pint.

This solution is injected through the duodenal tube to which a funnel is attached. About ten minutes is required for the injection and the fluid is injected warm. McNeil says that there is absolutely no danger to the patient from these injections.

As a preliminary measure, he advises keeping the patient on a liquid or semiliquid diet for two days before the injections; a saline purgative is given the night before.

One such injection is given daily for three mornings; in an adult, the last two injections are doubled in quantity. On the evening of each day on which an injection is given, the patient receives a high enema consisting of 1 to 5000 methylene-blue solution.

After three such treatments, the patient is allowed to go about his business, but is instructed to return at the end of a month for examination. At that time a saline purge is given and the resulting stool carefully examined for the parasites.

Intestinal Parasites in Foreign Students. In an article dealing with aliens in the United States, Edward J. Van Liere¹ says that the question naturally arises whether foreigners, especially those from the Orient, where parasites are so abundant, are a menace when entering this country. There is little doubt that the Chinese and Japanese who work the market gardens and do housework in California are dangerous to public health. An inspection in San Francisco in 1912 showed

(9) Southern Med. Jour., July, 1917.

(1) Jour. Amer. Med. Ass'n., Nov. 4, 1916.

infections as follows: Of 1,484 Japanese admitted, 581 had *Ascaris lumbricoides*; 452 *Trichocephalus dispar*, and 451 hookworm. Of 1,002 Chinamen examined, 789 had *Ascaris* and 588 had *Trichocephalus*. These figures show that the percentage of infection was rather high. The foreigners examined were not of the most desirable class, the lower castes being largely represented. On the other hand, the subjects at the University of Wisconsin undoubtedly come from some of the best foreign families, as only those with considerable means would be able to come to the United States for a college course. It may be safely assumed, therefore, that the results obtained are conservative as compared with those from more ignorant or poorer classes.

The feces of twenty male foreign students attending the University of Wisconsin were examined and ten (50 per cent.) gave positive results. The infections were as follows, the figures referring to the number of the patient: (1) Hookworm and *Trichocephalus dispar*; (2) *Hymenolepis nana*; (3) *Schistosoma japonica*; (4) *Ascaris lumbricoides*; (5, 6, 7, 8, 9, 10) *Trichocephalus dispar*. The infected individuals in several instances showed disorders connected with the presence of the parasites.

Thus the foregoing statistics indicate that 70 per cent. of the patients examined showed symptoms which parasitic worms might cause; 40 per cent. had severe cases of chloro-anemia, urticaria or eosinophilia. There is every reason to believe that in the absence of medical attention, it would have been only a short time until the parasites would have undermined the health of some of these persons, and some were certainly a danger to society.

Experiments on Ascaris Infections. As a continuation of work previously published, F. H. Stewart² presents here conclusions based on further experiments with mice and pigs. He states that if ripe eggs of *Ascaris lumbricoides* are swallowed by rats or mice they hatch. The larvae enter the bodies of the rodents either by boring into venules of the portal system or by ascending the bile-duct. They are found in the dilated blood

(2) Brit. Med. Jour., Oct. 7, 1916.

capillaries of the liver between the second and fifth days. The larva is in diameter three times the diameter of a red blood corpuscle of the mouse. It can not therefore pass through a normal capillary. The liver cells in the neighborhood of the larvae undergo rapid degeneration. The larvae are thus enabled to work their way into the hepatic venules and pass by the hepatic vein and vena cava to the heart and by the pulmonary artery to the lungs. In the lungs they are filtered off at the entrance to the capillary field. Embolism of the arterioles takes place, and the larvae pass with the effused blood into the air vesicles. They are found in the air vesicles on the sixth day, in the bronchi on the seventh day, and in the trachea and mouth on the eighth day after infection. It is probable that they emigrate in the saliva of the rodent on to food substances, such as bread. It has been shown that they can live for twenty-four hours on damp bread. The experiments which have been conducted so far tend to prove that the larvae from the lungs of rodents can infect the pig, and it is probable that in Nature infection of man and the pig takes place by food contaminated by rats or mice.

Longevity of Adult *Ascarides* Outside the Body of the Host. M. C. Hall^s reports that when he was in the service of the Federal Bureau of Animal Industry he made some tests to determine the length of time that the common round worm of the pig could live outside the body of its host.

A number of these worms had been collected and thrown into about a 5-per cent. dilution of liquor formaldehyde and left for a few minutes. They were taken out of the formaldehyde and nine of them placed in Kronecker's solution and nine placed in physiologic sodium chloride solution. The height at which the solution stood when made up was marked on the glass dishes containing them, and once a day distilled water was added to replace that lost by evaporation. The condition of the worms was noted every day except Sunday, and the room temperature noted every day except Sunday from the fifth day to the end of the experiment.

During the course of the experiment, the room tem-

(3) Jour. Amer. Med. Ass'n., March 10, 1917.

perature ranged from 27.5° to 30° C. (from 81.5° to 86° F.). The last survivor in the physiologic sodium chloride solution, a male, was alive on the fourteenth day after removal from the host, and was found dead on the fifteenth day. Three females survived for nineteen days in Kronecker's solution; two of these survived for twenty-four days, and one of these was alive on the twenty-sixth day after removal from the host and was found dead on the following day. In another experiment in which ten specimens of *Ascaris suum* were kept in physiologic sodium chloride solution, one worm was still alive on the fifteenth day. It appears, then, that ascarides may survive for fifteen days in physiologic sodium chloride and for twenty-six days in Kronecker's solution.

The particular interest which attaches to this experiment is its bearing on a very common idea in connection with anthelmintic treatment. It is quite commonly believed, and the belief is shared by many physicians and veterinarians, and is expounded in reputable medical literature, especially the older literature, as well as in the advertisements of commercial houses, that when a patient infested with worms is fasted for twelve or twenty-four hours, the worms become hungry as a result of this lack of food, and that when an anthelmintic is administered, especially when it is given in some such vehicle as milk, the hungry worms will ingest the anthelmintic and thereby become poisoned.

There are two or three objections to such a belief. In the first place, when these worms can survive for twenty-six days in such an unnutritious medium as Kronecker's solution, it is unlikely that they would suffer the pangs of hunger after twelve or twenty-four hours in contact with the collapsed walls of the intestine and the relatively abundant content of food, epithelial débris and secretions which is still present after such an interval. Moreover, it is known that the digested or partly digested food in the lumen of the host intestine is not the only food of parasitic worms, and it may constitute in some cases a very small part or no part at all. Garin says that nematodes of the digestive tract live at the expense of the wall of the digestive tract in all cases, and not on food in

the lumen. According to Garin, some worms (*Heterakis papillosa*) live on mucus and intestinal juices; others (*Oxyuris*, *Ascaris lumbricoides*, *Ascaris suum*) live on epithelial cells; others (*Ascaris rotundata*, *Physaloptera clausa*, *Habronema microstoma*) live on lymphatic cells and lymph; others (*Strongylus*, *Ankylostoma*, *Graphidium*, *Trichuris*) live on blood. He states that the attack on the mucosa may be mechanical (with teeth, etc., as in the case of hookworm) or chemical (by digestive secretions, as in the case of whipworms). Much remains to be learned in this connection, but it is known that such forms should suffer no inconvenience whatever during the period in which the host animal is deprived of food. Finally, it is not necessary to suppose that anthelmintics must be voluntarily ingested in order that the worms may be destroyed. It is likely that they are either ingested without volition or that they exercise their lethal effects in some cases by absorption, as may be the case with such volatile anthelmintics as chloroform.

In any case, the preliminary fasting, as well as the preliminary purgation, previous to anthelmintic treatment is, of course, a very desirable procedure. But its utility lies in the fact, says Hall, that it removes the bulky food mass which might otherwise protect the worm against the action of the anthelmintic.

Chemotherapy of *Lamblia* Infection. The wide distribution of *Lamblia intestinalis* in animals as well as man is discussed by V. L. Yakimoff¹ and his associates. It has been found in mice, rabbits, dogs, sheep and African hawks. They experimented with it in white mice by giving salvarsan to the infected animals, and report that salvarsan was effective in producing a cure. A 1 per thousand solution of salvarsan seemed to answer the purpose completely, no lamblia parasites being found in the intestines of the infected mice thus treated and killed in from one to three months later. The salvarsan did not seem to affect the *Octomitus muri* which was occasionally found in the mice, but its prompt success in eradicating the lamblia suggested to Yakimoff and his

(1) Russkiy Vrach, vol. 16, No. 10.

associates that it may prove effectual for lamblia dysentery and diarrhea in man. In their experience on the firing line in the Caucasus in 1915, numerous cases of dysentery and diarrhea were encountered in which neither the dysentery bacillus nor the ameba could be discovered and for which *Lamblia intestinalis* seemed alone to be responsible. In Yakimoff's laboratory, about 70 per cent. of the mice harbored the lamblia, but salvarsan treatment seems now to have exterminated the lambliosis among them. It was given by intravenous injection in 1:300 up to 1:1,000 solutions, allowing 1 c.c. of the solution to each 20 gm. of body-weight of the mouse.

Treatment of Lamblia Infections. By an examination of feces from 384 patients, H. M. Woodcock and W. J. Penfold,² at the King George Hospital, found infections in 220 instances, as shown in the accompanying table:

WITH PROTOZOA.

(Total Cases, 384.)

	No. of cases.	Percentage of total.	Percentage of positives.
Infected with Protozoa.....	98	25.5	...
FLAGELLATES:			
<i>Lamblia</i>	22	5.7	22.4
<i>Trichomonas</i>	14	3.6	14.2
<i>Macrostoma</i>	11	2.8	11.2
ENTAMOEBÆ:			
<i>E. coli</i>	57	14.8	58.1
<i>E. histolytica</i>	8*	2.0	8.2
COCCIDIA:			
<i>Isospora</i>	10	2.6	10.2

*This is inclusive of one case of liver abscess, in which the parasites were recovered only from the wall of the abscess.

In describing *Entamoebæ* the authors say that the most striking character about the cysts is their uniformly small size. They are generally spherical, from $7\frac{1}{2}$ to $8\ \mu$ in diameter, but occasionally are slightly ovoid, about 7 by $8\ \mu$; cysts larger than $8\ \mu$ were not seen at any examination of the stools. The cysts have a greenish, rather refractile appearance, and in the fresh condition no definite internal structure or nuclei can be made out.

(2) Brit. Med. Jour., March 18, 1916.

The cyst membrane is thin and does not show a double contour. After adding iodine solution one or two nuclei can usually be seen, and the chromidial blocks or masses,

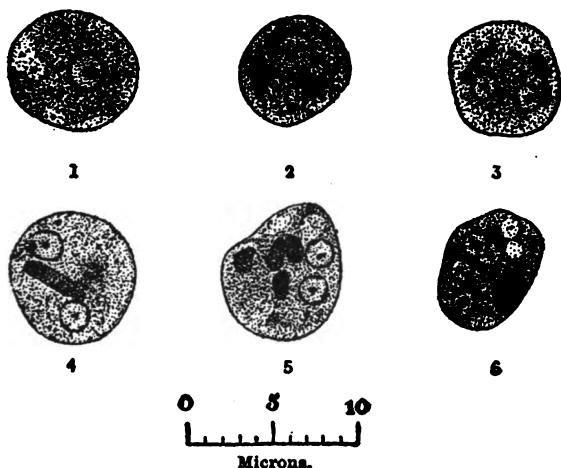


Fig. 17. *Entamoeba minuta* (from stained preparations). 1, Form preparatory to encystment. 2-6, Cysts with varying number of nuclei.

when present, generally take up the stain also, but these masses do not stand out so conspicuously in these cysts as do the chromidial bars in typical *histolytica* cysts. In permanent preparations stained with iron-hematoxylin the cysts show nearly always one (Fig. 17, 2) or two nuclei (Fig. 17, 3-5); only in a single instance (Fig. 17, 6) was a cyst with four nuclei found, although the preparations have been well searched. (In the figures the chromidial blocks or masses are stained up intensely.) Fig. 17, 1, shows an early stage in the encystment of this form. In addition to its smaller size, the nuclear character differs apparently from that of the nucleus of the cyst-producing, "*tetragena*" phase of *E. histolytica* in not showing a ring-like karyosome with a contained centriole-like body.

The authors think it quite likely that this form is really distinct from *E. histolytica*+*tetragena*, and consti-

tutes a third, independent form of *Entamoeba* occurring in man, either a distinct species or else a distinct variety.

Concerning the treatment of *Lamblia* infections, reference is made to a patient who also suffered from bacillary dysentery. *Lamblia* occurred in enormous numbers for a period of about a week. The patient was given betanaphthol 15 grains, with bismuth salicylate 20 grains, thrice daily, for some days. By the end of three weeks from the time of the first observation not a single flagellate or cyst was any longer to be found. Owing to other causes, this patient remained in the hospital for six months; during this time the stools were examined on several occasions. No sign of a flagellate infection, whether of active forms or cysts, was again found. This patient, therefore, is regarded as having been probably cured by the mixture.

Two other patients were treated with turpentine (*térébenthine*), following the opinion of various French workers as to its value. The dose was 10 minims, three times a day, for four or five days. This was followed by guaiacol carbonate, recommended by Dr. Thomson, 5 grains thrice daily, for a day or two before the stools were examined, but probably not long enough to have much effect. When the examination was made, in one case no cysts were found; in the other, after much searching, a few dead-looking cysts were seen. Four days later both stools were again examined, and in neither case were any cysts found. The patients were then sent out of the hospital. Recurrence is unlikely.

On the other hand, in two other cases, none of the remedies tried up to the present has produced any effect. Turpentine, guaiacol, and thymol have all failed.

Intestinal Protozoa in Soldiers. In a note dealing with intestinal protozoa as seen in a large number of soldiers in Saloniki war area, W. Roche³ states that the great spreaders of diarrhea and dysentery are flies. Heat and moisture are necessary for these pests to thrive. In the very hot spells, when everything was dried up, flies became a less menace in this zone. On the contrary, during a cold spell their numbers were diminished, and in these periods there was decidedly less diarrhea and

(3) Lancet, Feb. 24, 1917.

dysentery. The microscopic findings in the examination of stools are represented in the following table:

TABLE OF CASES EXAMINED, SHOWING THOSE INFECTED

Number of cases examined, 893; number of examinations, 1,425.	
E. F.	39
Non-pathogenic amebas (81)—	
<i>Entamoebae coli</i>	42
<i>Entamoebae coli</i> cysts.....	39
Pathogenic amebas (84)—	
<i>Entamoebae histolytica</i>	21
<i>Entamoebae histolytica</i> cysts.....	16
<i>Entamoebae minuta</i>	29
<i>Entamoebae minuta</i> cysts.....	18
Flagellate protozoa (217)—	
<i>Lamblia</i>	29
<i>Lamblia</i> cysts	44
<i>Tetramitus</i>	72
<i>Tetramitus</i> cysts	18
<i>Trichomonas</i>	45
<i>Cercomas</i>	9
Coccidia (18)—	
<i>Coccidia isospora</i>	15
<i>Coccidia eimeria</i>	3

Of the flagellate protozoa, *Tetramitus mesnili* was most commonly present and more often in its flagellate than in its cystic stage. *Lamblia intestinalis* was a common infection, the cystic form being more often present than the flagellate form. Five of the patients with lamblia infection were examined weekly during three months and despite all treatment they continued to discharge lamblia cysts up to the end of that time.

Trichomonas were found in comparatively few instances. This is peculiar, it is stated, as this parasite is so often present in the stools of people living in tropical and subtropical climates. *Coccidia* were found in eighteen stools.

The lamblia and tetramitus infection were the most difficult to get rid of. Calomel, bismuth, thymol, salol, turpentine, emetine, and Dale's double emetine were among the drugs tried without any results. Rectal irrigations with quinine, turpentine, eusol did not lessen the infection.

Protozoal Infections. An article concerning the occurrence of *Spirochaeta eurygyrata* is presented by J. W. Scott MacFie.⁴ He says that owing to the return to England of a large number of soldiers suffering from dysentery and diarrhea, a general interest has been evoked in protozoal organisms, which for many years have been familiar to every worker in the tropics. Among others, the spirochetes found in the intestines have come in for their share of attention, and the commonest species, *Spirochaeta eurygyrata*, has recently been described in detail by Fantham.

In West Africa the occurrence of small spirochetes has long been recognized, but the consensus of opinion has been that they were not pathogenic. Under abnormal conditions, in cases of dysentery or diarrhea, however, they were known sometimes to occur in myriads, and it was believed they might in these circumstances be a subsidiary cause of illness. In view of the revived interest in these organisms, this note on their prevalence in Europeans and natives in the Gold Coast Colony in Africa, is given.

Most of the specimens examined were taken from patients to whom a saline aperient had been administered for simple constipation, as a preliminary to surgical treatment, or for the purpose of ascertaining if helminth infections were present; in addition, fluid or semi-solid motions from cases of dysentery and diarrhea were searched, as well as some normal stools. These specimens were examined, both fresh and after fixation and staining. Leishman's stain and gentian violet were used—the latter when drawings were to be made for the purpose of measuring the length of the organisms, and the former when the structure of the cytoplasm was to be studied.

The article includes an extended description of the morphology of these organisms and a note on the geographic distribution. It is said that the fact that the spirochetes were most easily found after purgation or in persons suffering from diarrhea suggested that they frequented mainly the upper reaches of the bowel and were swept thence into the large intestine and rectum. A

(4) Lancet, March 3, 1917.

series of preparations made at an autopsy showed that the organisms were present in the stomach, and the small intestines at various points, in the cecum, and in the large intestine, but in this particular case they were plentiful in all of these situations. In a second case they appeared to be most numerous in the cecum, but were nowhere abundant.

Concerning the mode of infection, MacFie says that in the case of an organism so widely distributed as *Spirochaeta eurygyrata* was found to be, there can be no difficulty in the spread of the infection, directly or by the contamination of food. When exposed to the action of 0.2 per cent. hydrochloric acid in laboratory experiments, the spirochetes did not appear to be injuriously affected, for some hours at any rate; their activity often seemed to be increased and at autopsies smears made of the stomach contents showed that they were present in this part of the gastro-intestinal tract. Infection from man to man by means of spirochetes themselves is, therefore, possible and probable.

Concerning the pathogenicity, these spirochetes have been found at Accra in the feces of every individual, either European or native, examined for these organisms. As the majority of the persons examined were in a state of normal health, the pathogenicity of this spirochete must be very slight, if indeed it is at all harmful. As a rule, the spirochetes appear to be non-pathogenic—that is to say, their presence is not incompatible with a normal state of health, but under certain conditions they multiply so enormously that it is difficult to believe that they can be entirely benign.

A monkey, a cat, rat, sheep, cattle, goats, and pigs were found to harbor organisms morphologically indistinguishable from *Spirochaeta eurygyrata*, the species found in men. H. F. Carter examined both dysenteric and non-dysenteric patients, and found the spirochetes in 56.5 per cent. of the former and 41.0 per cent. of the latter. These results are of interest when compared with those obtained in West Africa. It still remains to determine the prevalence of the infection in persons who have resided in temperate regions only.

Treatment of Chronic Protozoic Enterocolitis as Encountered in the Northern United States. In the temperate zone, says Frank Smithies,⁵ chronic enterocolitis associated with protozoa in the stools is more frequent than is generally understood. In an analysis of the findings in 1,000 stools examined at the gastro-enterological laboratory at Augustana Hospital, Chicago, viable protozoa were demonstrated in the dejecta from ninety-three patients. These patients came mainly from the northern half of the Central States. There were from Illinois twenty-nine, Iowa sixteen, Wisconsin thirteen, Nebraska eight, Michigan seven, Indiana four, South Dakota two, Arkansas two, Ohio two, Texas two, Kentucky one, Northern California one.

In the majority of patients, the intestinal canal seemingly had been infected as a consequence of partaking of water contaminated by sewage, carelessly washed, manure-forced garden-truck (lettuce, celery, radishes, tomatoes, mushrooms, onions, cabbage, etc.) or insect-befouled fruits (bananas, especially). It is quite likely that the sewage and dung infections resulted from protozoa carriers (soldiers or civilians) who at some time had encamped or resided in Mexico, South America, Cuba, the Philippines, the Orient, or in the Southern States bordering Mexico. During the past twenty-five years, the northern United States has had ample opportunity to become widely infected as a consequence of the military, commercial and educational activity of Americans in these tropical or semi-tropical localities.

In the cases of chronic protozoic enterocolitis studied in the author's clinic there was achylia gastrica in 43 per cent., subnormal hydrochloric acidity in 36 per cent., and normal or increased gastric hydrochloric acidity in 21 per cent. In one patient with a most pronounced infection with cercomonads and trichomonads the free hydrochloric acid reached 86. In 70 per cent. of the cases, the stools revealed tryptic

(5) *Medicine and Surg.*, July, 1917.

digestion, and in 29 per cent. there was deficient amylolytic ferment.

Anemia of so pronounced a grade as to suggest pernicious anemia was present in nineteen cases. The anemia commonly observed is of the secondary type, such as is evidenced in chronic intoxications, as nephritis, malnutrition, malignancy, etc. In this series of cases, the hemoglobin averaged 70 per cent., the red cell count, 3,120,000 and the leukocytes 8,400. There were sixty-nine cases in which eosinophilia reached or exceeded 3 per cent.; there were eleven cases in which it ranged between 8 per cent. and 14 per cent. There was one instance of amebiasis and trichomoniasis in which the eosinophile estimation was 18.5 per cent.

It is very important that the type of infecting protozoa be determined before successful treatment can be instituted. This is possible only by microscopic examination of the freshly passed stool. High power objectives should be used and the slide upon which the specimens are studied should be kept heated. Examinations of many stool specimens is necessary to prove or exclude multiple infections. The effect of protozoacides can only be gauged by daily study of the warm, freshly-passed stool. It is necessary to urge here that this daily stool study forms one of the most essential details of the treatment of protozoic enterocolitis. The microscopic findings absolutely control therapeutic management; they are in fact, the only control.

In this series of ninety-three cases, the types of infecting protozoa were commonly multiple. Their incidences is indicated by the following table:

LIST OF INFECTING PARASITES.

<i>Cercomonas intestinalis hominis</i>	36
<i>Trichomonas intestinalis hominis</i>	21
Entamebas	
Histolytica stage	17
Tetragena stage	6
Unclassified	4
Amebas total	27
<i>Lambliu intestinalis hominis</i>	5

<i>Megastoma entericum</i>	2
<i>Balantidium coli</i>	2
Grand total of cases.....	93

COINCIDENT INFECTIONS.

Cercomonas with entameba.....	12
Trichomonas with entameba.....	14
Cercomonas, trichomonas and entameba.....	4
Trichomonas and cercomonas.....	8
Cercomonas and lamblia.....	3
Cercomonas, trichomonas and lamblia.....	2
Trichomonas, cercomonas and megastoma.....	1
Trichomonas and balantidium.....	2

It is evident that in the majority of instances, medical treatment must be directed against two types of parasites—namely, the entameba group and the flagellates.

The clinical symptomatology associated with these two types of protozoa, in association with enterocolitis, differs somewhat. It is summarized as follows:

SUMMARY OF CLINICAL SIGNS AND SYMPTOMS.

(Figures stand for number of cases.)

	Parasite					
	Ameba	Cerco- monas	Tricho- monas	Lamblia	Mega- stoma	Balan- tidium
Diarrhea	24	33	20	5	2	2
Constipation	1	2	1	0	0	0
Normal stools.....	2	1	0	0	0	0
Abdominal pain.....	21	30	17	4	2	1
Dyspepia	15	28	21	5	1	2
Weight loss	17	30	21	3	2	2
Achylia gastrica.....	13	12	11	2	1	1
Subnormal acid.....	8	14	8	2	0	1
Normal gastric acid.....	6	10	2	1	1	0
Anemia	26	31	18	4	2	2
Eosinophilia (above 3 per cent.)	19	27	15	2	1	1
Blood in stools.....	14	17	16	3	2	2
Fever	4	1	2	0	0	0
Chill	2	3	2	1	0	1

Study of the above summaries indicates that in this affection, treatment lies in two main directions—namely: (a) *Measures for freeing the alimentary tract from protozoa*; (b) *the management of dyspepsia and mal-*

nourishment associated with enterocolitis. It is advisable, Smithies says, to consider the two steps separately.

(a) *Measures for Freeing the Alimentary Tract from Protozoa.*—A preliminary preparation of the intestinal canal enables one quickly to bring about its relative sterilization. In Smithies' clinic, these patients are placed on liquid diet for two days before medical treatment is begun. This permits of the bowels being freed from firm residues. Each morning, they receive a glass of citrate of magnesia solution. *The aim of specific medicines is (a) to render inert protozoa infecting the intestinal contents, and thus prevent infection of the mucosa, and (b) to destroy organisms already lodged within the mucous membrane.* Successful therapy depends upon proper isolation of the infection parasites—entamebas are particularly susceptible to ipecac or its alkaloid, emetine, while flagellate or ciliated protozoa are slightly affected by these drugs, but are readily destroyed by calomel. Thymol is effective against both parasites.

(1) In the *entameba* cases, the patient is put to bed on liquid diet, with hot pads moistened in boracic-alcohol mixture over the abdomen (to prevent colicky pains or abdominal discomfort). He is then given by mouth a 10-gr. tablet of the aluminum salicylate of ipecac ("alcresta") every hour and $\frac{1}{2}$ gr. of emetine hydrochloride hypodermically every four hours for two days. Five-grain salol-coated pills of ipecac may be administered every two hours if "alcresta" is not available. If the salol coating of the pills is not "pinholed" this method of administration is very satisfactory. Beck has suggested administering ipecac preparations directly into the duodenum through one of the commonly employed duodenum tubes. Two-grain capsules of methylene blue given every hour for three days also appear to be of service in instances of multiple infection.

If the stools show diminution of the parasites, the dose of ipecac and emetine is then reduced by one-third, and this continued for another two-day period. No reduction is made if the parasites are still very abundant or are very active. Usually by the end of the first week,

the patient is taking emetine, $\frac{1}{3}$ gr., hypodermically, twice daily, and 10 gr. of ipecac ("alcresta") four times daily. The diet should be very soft or liquid. The treatment is continued even when no parasites are seen.

Accompanying the medicines given by mouth, the colon is carefully lavaged with 4 quarts of hot normal salt solution or a solution of quinine (1:3000) and thymol (1:5000) in normal salt solution night and morning. A 1:1000 solution of methylene blue is also of service, although not so practical on account of its staining linen, etc.

On the sixth day, the patient is put on fat-free diet for twenty-four hours. Fat-free diet is necessary to prevent the large doses of thymol from producing toxic damage. On the evening of the seventh day, 30 gr. of thymol in honey are administered at 8 p. m. and again at 10 p. m. At 6 a. m. the following morning, the patient gets 2 oz. of Epsom salts in hot water, and all that morning frequent drinks of black coffee, fat-free broth, or malted milk.

During the second week, the emetine, ipecac, and bowel irrigations are continued, and usually on the tenth day from the beginning of the treatment, two doses of 15 gr., each, of thymol (preceded by twenty-four hours of fat-free diet) are given in the evening. A diet similar to the following is allowed:

- | | |
|-------------|--|
| 7:30 a. m. | 1 cup parboiled milk.
1 cup strong black tea or cocoa not very sweet.
2 egg yolks—hard boiled, then crushed and seasoned.
3 pieces zwieback. |
| 10:00 a. m. | 3 graham crackers.
1 cup strong black tea with sugar.
1 baked potato (interior mealy) or 3 ounces |
| 12 Noon | 1 cup beef broth.
4 ounces rare beef or well-done lamb or chopped beef.
1 baked potato (interior mealy) or 3 ounces
mashed potatoes.
2 pieces zwieback.
3 to 4 ounces rice, tapioca, sago, chocolate pud-
ding, blanc mange, firm custard, chocolate
cake, cottage cheese, baked apple. |
| 3:00 p. m. | 1 glass parboiled milk.
Graham crackers if desired. |

- 6:30 p. m. 1 pint parboiled milk (not boiled) with cooked rice in it.
1 cup strong black tea or cocoa (not too sweet).
2 hard boiled egg yolks crushed and seasoned.
2 pieces zwieback with butter.
- 9:00 p. m. 1 glass buttermilk or parboiled milk.

Daily examinations of the warm stools usually indicate no parasites by this time, and the diet may be increased according to the patient's desires, providing it is low in protein and not very bulky. If parasites persist at the end of two weeks, then, after thorough colon lavage with hot normal saline solution, from 500 to 1,000 c.c. of filtered commercial kerosene are given by rectum, slowly. The external parts are greased with carbolated vaseline and effort is made to have the patient retain the kerosene for at least one hour. Smithies has never seen any harmful effects follow the use of kerosene. It has proved very efficacious in ridding the bowels of persistent infection (entamebas and lamblia).

(2) When *flagellate protozoa* are the infecting organisms, the treatment is substantially as outlined above for entamebas, except that emetine and ipecac are not used, unless there is a concomitant amebiasis. The flagellates are readily destroyed by the administration of evening doses (5 to 15 gr.) of calomel followed by 2 oz. of Epsom salts the next day. These doses of calomel are repeated about every five days, according to the indications furnished by the stool examinations. The flagellates are usually less persistent than the entamebas (with the possible exception of lamblia).

(b) *The Management of Dyspepsia and Malnourishment Associated with Enterocolitis.*—When the protozoa are no longer demonstrable in the freshly passed stool, then local treatment of the enterocolitis by large doses (30 gr.) of bismuth subnitrate or salicylate given five times daily should be carried out. Emetine and ipecac should be continued for at least six weeks; the ipecac alone for three months. The bowel irrigations are usually stopped at the end of the third week. The general state of the patient is taken care of according to indication—hydrochloric acid after meals, if the gastric

juice is low or lacking in acid; iron and bismuth, if anemia is present.

DIET.

- 7:00 a. m. 1 pint of skimmed milk and 2 zwieback.
 9:00 a. m. 2 pieces of well cooked toast without butter.
 Juice of 1 sweet orange or $\frac{1}{2}$ grapefruit, or $\frac{1}{2}$ of ripe melon, or baked apple or dish of apple sauce.
 1 dish of well-cooked cream of wheat, farina or oatmeal with cream and sugar.
 2 very soft poached eggs with butter.
 11:00 a. m. 1 cup of bouillon (2 cubes) and 3 crackers.
 1:00 p. m. This should be the big meal of the day.
Meats—rare if possible—such as beef, lamb, well cooked or white meat of chicken. Any kind of fresh-water fish, but it should never be fried. Limit to 4 ounces.
Vegetables should be cooked or well washed in bacteriologically clean water. Well-cooked spinach, cauliflower, carrots, squash, peas (hulled), string beans, Brussels sprouts, baked or mashed potatoes (in moderation). rice, with gravy.
 Simple puddings made from cereals, cornstarch, gelatine, well cooked fruit sauces, simple cakes.
 No white breads—all breads should be made from dark flour and preferably should be at least 24 hours old.
 1 pint of skimmed milk taken hot.
 4:00 p. m. 1 glass of hot malted milk or parboiled whole milk or cocoa.
 Two graham crackers.
 7:00 p. m. A light supper consisting of vegetable soup, toast, soft eggs and plain puddings, or sauces made from fruits.
 Simple cake may be eaten if desired.
 1 pint of skimmed milk and $\frac{1}{2}$ gill cream taken hot.
 Bedtime—1 glass of malt marrow or hot malted milk or cocoa.

(c) After-treatment.—Smithies' study of specimens of gall-bladders and appendices removed at laparotomy indicates that in these parts of the gut cysts of protozoa may lurk for years. Reinfection of the bowel is thus possible. Consequently, if these organs have not been removed, Smithies insists that these patients have stool

examinations at least three times a year, and that they go through an abbreviated course of treatment similar to that outlined. Only by so doing, he believes, can protozoa carriers be eliminated or reinfection of so-called cured cases be prevented. There are cases he says in which cholecystectomy and appendicectomy are required before recurrent infections are eliminated.

Hookworm Disease—Diagnosis and Treatment. An article concerning hookworm disease and its diagnosis and treatment is presented by W. C. Billings and J. P. Hickey,⁵ of the United States Public Health Service.

They state that observations made on Orientals in the United States Immigrant Hospital, at Angel Island, Cal., extending over a period of over three years, convinces them that whenever practitioners are consulted by an Oriental a microscopic search for hookworm ova should be made just as much a part of the routine examination, in all cases in which the diagnosis is not apparent or is at all doubtful, as is the routine examination of the urine, the blood or the sputum.

From Sept. 22, 1910, to Jan. 1, 1913, 6,428 stools of Oriental aliens were examined in the hospital, and 3,320, or over 50 per cent., were found to be infected with either *Ankylostoma duodenale* or *Uncinaria Americana*.

Many of those who presented themselves for examination were robust and athletic in appearance, but in the feces by microscopic examination positive results were found. It may be that, owing to a mild infection, or possibly because of immunity conferred by generations of hookworm-infected ancestors (assuming that the anemia of hookworm disease is the result of the presence of a toxin), these people will themselves never suffer to any great extent because of their infection; but they are nevertheless foci of danger if allowed to remain uncured.

The result of the tabulation made by these authors bears out the impression that, if accurate results are to be obtained, the general appearance of the person must be quite disregarded and the microscope used as a routine measure in every case. Because of the importance of this particular measure, an outline of the technique used in this work is quoted in full.

(5) Jour. Amer. Med. Ass'n., Dec. 23, 1916.

1. Take a piece of (preferably) formed stool, approximately the size of a walnut, place it in a porcelain cup, and after adding about 60 c.c. of cold water, thoroughly break up the mass with the aid of a wooden tongue depressor. When the suspension is as complete as possible, destroy the tongue depressor. If the stool is liquid, add an equal bulk of cold water and mix as directed above.

2. After placing over the mouth of the cup two or three layers of wide mesh surgical gauze, strain a portion of the contents of the cup into a centrifuge for ten seconds at full speed (which means 2,000 revolutions a minute). The gauze is thrown away and a new piece used for the next specimen. The cup is emptied of its remaining contents and thoroughly scalded.

3. Remove the tube from the centrifuge, and without disturbing the sediment, pour off the supernatant liquid and refill with cold water to about three-fourths the capacity of the tube.

4. Place a thoroughly clean rubber pad over the mouth of the tube, hold in place by the thumb, and shake vigorously. When preparing two tubes at the same time, extreme care will be necessary that the rubber pads are used on their respective tubes at each shaking.

5. Again centrifuge for ten seconds at full speed.

6. Pour off supernatant fluid as described above, and refill with cold water. Again shake.

7. Centrifuge for ten seconds at full speed.

8. Pour off supernatant fluid, leaving about one-half inch overlying the undisturbed sediment. The specimen is now ready for a microscopic examination.

As an aid in the diagnosis of ova the accompanying table for differentiation is given:

The accompanying illustration (Plate V) shows to some extent the differences between the parasites which are liable to be confused with *Ankylostoma duodenale* or *Uncinaria Americana*.

Concerning the treatment of this condition, the authors state that thymol as an anthelmintic has been used almost universally throughout the United States in the treatment of hookworm disease and it was used exclusively in this hospital until one year ago, when oil of

PLATE V.



Note comparative size: *a*, *Ankylostoma duodenale*; *b*, *Trichostrongylus instabilis*; *c*, *Trichocephalus dispar*; *d*, *Ascaris lumbricoides* (with albuminous covering).—Billings and Hickey (see page 257).

	Shell.	Shape.	Contents.	Average size, mm.
<i>Ankylostoma duodenale</i> ..	Thin	Oval	Grayish	0.06 by 0.04
<i>Trichostrongylus instabilis</i>	Thin	Oval, flattened on one side, more pointed at one pole...	Dark gray to brown	0.076 by 0.0415
<i>Schistosoma japonica</i> ..	Thin; sometimes double contour.	Oval.....	Pale yellow to yellowish brown ; granular or containing miracidium	0.074 by 0.053
<i>Ascaris lumbricoides</i> ..	Thick; double contour*	Round or oval	Bile stained.	0.065 by 0.045

*Applies when devoid of albuminous covering.

chenopodium was substituted. Since that time, owing to the encouraging results obtained, this oil has been adopted as the regulation treatment to the exclusion of all others, the oil being of the variety known as the Baltimore oil. Compared with thymol, oil of chenopodium gives markedly better end-results, and its value is further enhanced by the facts that not only it is followed by fewer disagreeable after-effects but with its use no dietetic precautions need be exercised either before or during its administration.

The routine course of treatment for adults as used in this work was as follows:

Preparatory treatment: At 7 a. m., magnesium sulphate, saturated solution, 60 c.c., is given. At 7 p. m., sodium sulphate, saturated solution, 90 c.c. The next morning, chenopodium is commenced, proceeding as follows: 7 a. m., oil of chenopodium, 15 drops. 9 a. m., oil of chenopodium, 15 drops. 11 a. m., oil of chenopodium, 15 drops. 1 p. m., castor oil, 18 c.c.; chloroform,

2 c.c. 1:30 p. m., plain castor oil, 30 c.c. 2 p. m., a cup of hot tea.

Oil of Chenopodium and Chloroform as Anthelmintics. A series of animal experiments have been made by M. C. Hall and W. D. Foster⁶ to determine the value of certain substances as anthelmintics. In this preliminary note they present chiefly the conclusions reached; the detailed report is to be published later. They found that oil of chenopodium has a very high co-efficient of efficacy against ascarides, and among the drugs tried it was found more effective in a single therapeutic dose against these worms than any other drug. Furthermore, its efficacy against ascarides proved greater than that of any other drug against various other parasitic worms with which they experimented. It should be given with castor oil and followed with castor oil, the drug being administered on an empty stomach, in order to secure the best results and to give the patient the maximum amount of protection from the local and systemic effects of the drug. Chloroform, however, has a higher co-efficient of efficacy against hookworms than oil of chenopodium or any other drug studied in this work. It can be given internally in castor oil in therapeutic doses with a degree of safety that compares favorably with that of the classic, and, according to these experiments, less effective remedies.

The authors compared it with santonin, thymol, turpentine, areca nut, tartar emetic, ether, chloroform, coal tar phenols, spigelia, a number of common purgatives, which have been said to have anthelmintic properties, and two samples of the latex of *Ficus laurifolia*—one of which, however, did not accord with the description of this substance—and have found that oil of chenopodium properly administered is a more effective and dependable remedy for ascarides than any of the others. In fact, it comes close to being 100 per cent. effective.

Concerning chloroform, they state that its toxic effects upon the heart, kidneys, and liver are obtained by administering it as an anthelmintic to a degree similar to that resulting from the use of chloroform as an anes-

(6) Jour. Amer. Med. Ass'n., June 30, 1917.

thetic. In the interest of the patient's safety, an anthelmintic dose of 2 or 3 c.c. of chloroform should not be repeated within three weeks, and certain lesions of the liver, kidneys and heart would be contra-indications. It is also true of chloroform, as of other anthelmintics, that patients with massive infestations who are in very poor physical condition and whose vitality is much lowered should be put in the best possible physical condition before a weakened digestive tract, with the lesions due to hookworm attacks, is subjected to the shock of anthelmintic treatment.

COLITIS.

Some Phases of Chronic Colitis. At the annual meeting of the Medical Society of the State of Pennsylvania, Edwin Zugsmith⁷ of Pittsburgh read a paper on this subject.

It is probable, he said, that the persistent showing of any amount of mucus justifies the diagnosis of colitis. There is on record a report of a single evacuation of several pounds of mucus. Toxic materials entering the body because of the loss of the selective power of the colon in absorbing material cause anemia and nervous irritability often diagnosed as neurasthenia. Colitis is often a process secondary to infection of gums, teeth, throat and nasal sinuses, of the bronchial tubes, probably of the gall-bladder, incompetent functioning power of the liver and pancreas, dietetic errors, and abuse of laxatives. The relationship of colitis and appendicitis, Zugsmith says, is very close. The tendency to progressive stasis about the cecum subsequent to appendectomy indicates the need of after-treatment in such cases, with particular attention to the colon. While colitis is often a secondary process, it may give rise to other conditions; some of the worst cases of inflammatory rheumatism, the author believes, undoubtedly have their origin in a diseased colon. Colitis is sometimes confused with other diseases, chiefly because the stool examination is omitted. A careful examination would reveal tenderness in the right iliac fossa and would often save the physician from

(7) Meeting held at Scranton, Pa., September, 1916.

the embarrassment of a mistaken diagnosis of appendicitis. Some cases of colitis are diagnosed ulcer of the stomach and duodenum on the history of pain after eating. The teaching that such pain means ulcer is fallacious. The proximity of the hepatic flexure to the gall-bladder also confuses diagnosis. Zugsmith says that colitis is often confused with neurasthenia through carelessness. The disease is essentially chronic. That it cannot be cured is a pessimistic belief without any justification. With proper food, hygiene and medication, many patients are cured and the majority are greatly improved. The most efficient guide against dietary errors is the frequent microscopic examination of the stools. Next in importance to diet in the treatment are hygienic regulations. Olive oil injected into the sigmoid at night, half a pint or more, and allowed to remain over night, aids more than any other remedy in overcoming constipation.

SPRUE.

Etiology. The results obtained by the investigation of several hundred cases of sprue in China are the basis of an article on the etiology of this disease by H. Dold.⁸ This study was begun in 1914. In describing the disease as seen in China, Dold says that the prominent feature of a fully developed case of sprue is the character of the diarrheal stools. The feces are voluminous, foamy, *i. e.*, filled with numerous gas bubbles, acid in reaction, and light, usually grayish-white, in color. The diarrhea is accompanied by flatulence, the feeling of a blown-up stomach, burning sensations in the upper part of the digestive tract—esophagus, mouth, tongue—and signs of inflammation. Furthermore, the liver is small, and there are anemia and wasting.

Two theories have been advanced with regard to the etiology of sprue. According to one, it is a deficiency disease similar to pellagra; according to the other, sprue is an infection. From personal observations made in China, Dold is inclined to support the latter theory. He believes that a bacterial cause underlies the pathology of sprue.

(8) Med. Record, Feb. 3, 1917.

In order to throw light on the point in question, a comparative study was made on the frequency of blastomycetes and other acidophil organisms in normal feces, in diarrheal stools of non-sprue character, and in the diarrheal stools of sprue.

In a summary of results obtained by the investigation of stools, the author states that while blastomycetes from normal feces could be grown in only 7.5 per cent., and from diarrheal stools of non-sprue character in 16 per cent. of the cases examined, *from all the stools of sprue character, either blastomycetes or oidia or both were readily isolated in great numbers.*

The conclusions reached from this work are given as follows:

A bacteriologic analysis of some hundred sprue stools in China shows that either blastomycetes or oidia, or both, appeared in these specimens in greatly increased numbers, as compared with normal feces or diarrheal stools of other origin.

Regarding the oidium, the results appear to coincide with the findings of Bahr in Ceylon and those of Ashford in Porto Rico; as to the blastomycetes, they confirm the statement of Le Dantec.

The blastomycetes as well as the oidia are acidophil in character and possess great fermenting power; they produce large quantities of acid and gas from carbohydrates.

White mice fed with pure cultures of the blastomycetes or oidia develop within a short period of time a type of diarrhea which closely resembles the typical diarrhea of sprue. The animals show marked emaciation and die within a few weeks. There are considerable differences in resistance.

These results tend to show that sprue is a bacterial disease, not, however, necessarily due to a single bacterium, but frequently caused by different microbes having identical biologic and pathologic effects.

The primary factor in sprue appears to be a disturbed balance of the bacterial activity in the intestinal tract. Organisms of high fermenting power, blastomycetes, oidia, and possibly others, gain the upper hand. These organisms produce large quantities of acid and gas, prin-

cially out of the ingested carbohydrates. The composition of the food, therefore, must greatly influence the condition. This is confirmed by clinical experience. In this sense sprue may be called a diet disease.

The emaciation and anemia observed in sprue may be explained by the long-standing diarrhea, the great loss in carbohydrates, the disturbed fat resorption, as proved by microscopic inspection of the feces, and possibly also by the resorption of toxic intestinal, bacterial products, as suggested by the animal experiments described.

The characteristic and striking decrease in the size of the liver, which occurs even in an early stage of the disease, may be regarded in part as a direct consequence of "carbohydrate hunger," the carbohydrates ingested being quickly and extensively split up into acid and gas, so that little remains for resorption and deposition in the liver in the form of glycogen.

Sprue in North Queensland. This article is written by A. Breinl and H. Priestley,⁹ of the Australian Institute of Tropical Medicine. They define sprue as a chronic inflammation of the alimentary tract affecting principally the tongue, esophagus and small intestine, which leads to degenerative changes in the epithelial layer, to formation of ulcers and to atrophy of the liver. The most characteristic features of the disease are the passing of numerous large, frothy, clay-colored stools, the intractability of this diarrhea to ordinary treatment, the general wasting and the intermittent course.

As to distribution, the disease is most prevalent in the East. Its presence has been known for a considerable time in Java, China, India, Ceylon and the Philippines, but lately cases have been described from other tropical and subtropical countries, as Porto Rico and the southern parts of the United States.

The onset is insidious, and the early stage may last for weeks or months. As a rule the first definite symptom is soreness of the tongue. A few small rounded vesicles of whitish color appear on the edge and tip of the tongue, often on the frenum and occasionally on the mucous membrane of the cheek; these vesicles break down

(9) Med. Jour. Austral., February, 1917.

later, forming shallow ulcers with ragged edges, which persist for a varying period.

Similar inflammatory and atrophic changes affect the epithelial layer of the esophagus, and cause one of the earliest symptoms of sprue—the burning sensations experienced when the patients swallow food.

The gastro-intestinal symptoms, however, dominate the clinical picture from the earliest stages. Obstinate indigestion, abdominal uneasiness after taking food, distention and flatulence, and belching of gas, persist in a varying degree during the whole course of the disease. Diarrhea is present to a greater or less extent from the earliest to the latest stages, but the character of the motions does not remain the same throughout the disease.

The skin invariably shows changes. Even during the early stages the complexion is sallow, and pigmented areas appear on the forehead and cheeks and on the extensor surfaces of the forearms, resembling the pigmentation occurring in pregnancy. The general atrophy affects the whole of the organism, and patients in the latest stages of sprue appear aged much beyond their years.

The urine in sprue patients does not show any characteristic changes.

The nervous system does not show any anatomic lesions, but marked functional changes. A complete alteration in disposition is a somewhat constant and definite change, and seems to be indicative of more than the familiar irritability of dyspepsia.

In making a differential diagnosis of sprue, pernicious anemia and its accompanying diarrhea and some diseases of the pancreas are of much importance. Pellagra in several of its manifestations resembles sprue, and may offer difficulties in the differential diagnosis. In this disease, however, as a rule the skin lesions dominate the clinical picture, and their localization is pathognomonic, affecting those parts of the body exposed directly to sunlight, and show a symmetrical distribution.

Morbid anatomy as given in this paper is based upon autopsy reports. The authors state that corresponding to clinical manifestations characteristic lesions are found throughout the alimentary tract. The tongue is denuded

of its surface epithelial layer. The mucous membrane of the esophagus is hyperemic and covered with mucus; here and there are small roundish shallow ulcers with irregular edges. The stomach does not show any lesions. The small intestine is hyperemic, its wall throughout appears thinner than normal and roundish ulcers occur in the lower jejunum and ileum of varying diameter (up to 2.5 c.m.) with irregular crateriform edges. The intestinal wall at the base of the ulcer is very thin, and of paper-like appearance. The base of the ulcer is either glistening (probably due to an attempt at regeneration of the epithelium) or covered by an adherent layer of thick mucus. Similar ulceration has been noted in the large intestine.

In two post-mortem examinations the large intestine was the seat of extensive pathologic change. The wall was considerably thickened and covered with diphtheritic membrane. Perforation had taken place, resulting in localized peritonitis with extensive adhesions in the neighborhood, so that on opening the abdomen the organs and intestinal coils were matted together, recalling the appearance of a late stage of tuberculous peritonitis.

The liver is invariably reduced in size and is microscopically normal in structure, except for a considerable dilatation of the bile-ducts.

The pancreas is sometimes atrophic and fibrosed, at other times it is of normal appearance. None of the other organs of the body show any changes beyond those of general atrophy.

Concerning the prognosis, the authors say that in general improperly or untreated sprue is a disease with a serious outlook. The patient goes from bad to worse and finally succumbs to the general marasmus. If properly treated, cures may be effected, but relapses are frequent and more likely if the patient returns to the endemic area. Patients are, therefore, always advised not to live again in an area where sprue is endemic. As to etiology, the authors say that they have been able to cultivate yeast from every case of sprue under their care, from the tongue and feces, and on the occasion of two post-mortem examinations from every part of the intestinal tract. Considerable difficulties were encountered in isolating the

yeasts in pure culture, until use was made of the fact that acid media are favorable for the growth of yeast, but inhibit development of the majority of bacteria. After trials of various acidified, solid and liquid media satisfactory results were obtained with 0.5 per cent. tartaric acid in 1 per cent. glucose peptone water.

All attempts in the present work to produce sprue in laboratory animals has been unsuccessful, though such experiments have been in progress in the authors' laboratory over a number of years. Attempts have been made to produce in different ways a disease analogous to sprue in monkeys, dogs, cats, rabbits, guinea-pigs, rats and mice, but without success.

The treatment of sprue so far as a complete cure is concerned is at present unsatisfactory. Drugs which one observer found to give excellent results did not influence the course of the disease in the hands of others. It would seem of no avail to enumerate all the drugs which have been recommended, but the latest two additions to the list, namely, colloidal argenticum, and emetine may be mentioned, both of which drugs were used in this work. Colloidal argenticum was administered as advocated by Cantlie in doses of from 30 to 60 minims early in the morning on an empty stomach. Other patients received one grain of emetine daily for three weeks, but neither drug influenced the disease in any way.

In routine treatment the authors prescribed as a rule a simple alkaline mixture, such as glyco-thymoline in dram doses three times daily, and it apparently relieves, to a certain extent, the flatulence and abdominal discomfort.

In reference to the dietetic treatment the present experience, generally speaking, confirmed that of most other observers, namely, that a diet consisting of milk only must be rigidly adhered to in the early treatment of sprue. At the commencement three pints of fresh undiluted milk are prescribed for the patient, about eight ounces being given every three hours, and the patient is advised to drink it slowly or, better, to suck it through a straw or sip it with a teaspoon. The amount of milk is gradually increased, an extra pint being added every

four or five days, depending on the general progress. The patient is strictly kept in bed.

After an interval ranging from days to weeks, when the patient feels decidedly better, bananas and grapes and strawberries are given if these articles are obtainable. Apples, pears, mangoes and oranges were found not to be well borne.

After the stool has become formed, for at least two weeks, stewed apples and junket are allowed, later still minced meat once a day, and green vegetables and buttered toast.

Gastro-Intestinal Findings in a Case of Sprue. In the case reported by T. R. Brown,¹ of Baltimore, the most striking features were: First, the persistence of the complete absence of pancreatic secretions, not only during the stage of acute illness, but even after the patient seemed absolutely well; second, the essential rôle of the constant administration of pancreatic extract by mouth in the treatment of the disease; third, that whatever the cause of sprue, and at present it seems probable that it is due to an infection with monilia, the lack of pancreatic secretion seems persistent and fundamental, the absence of gastric juice variable and accidental; fourth, that so long as a patient suffers from this pancreatic achylia he can in no wise be considered cured, although clinically he is apparently well; and the ultimate outcome must still remain doubtful.

BOTULISM.

Botulism. An attack of botulism is reported by Schede² as occurring in a family who had eaten raw ham. The pig had been killed six months before. About eighteen hours after the ham was eaten, symptoms of botulism became apparent in the mother and two boys aged 10 and 12. The mother and the older boy died; the other recovered. The father who had eaten most freely of the ham was not affected. The only gastro-intestinal disturbances were nausea and vomiting which the older boy suppressed. Extreme prostration, dryness of the

(1) Bull. Johns Hopkins Hosp., October, 1916.

(2) Med. Klinik, Dec. 10, 1916.

mucous membranes, difficulty in swallowing and in speaking, diplopia, ptosis, absence of the knee-jerk, paresis of the bladder sphincter and other symptoms showing extensive involvement of the central nervous system were the most pronounced symptoms until the respiratory center became affected. In the two fatal cases, death occurred from paralysis of the respiratory respiration.

As it was impossible to secure any antitoxin serum, diphtheria antitoxin was tried but without result. Schede gave pilocarpine 0.01 gm. to combat the dryness of the mucous membrane, but it produced alarming symptoms from over-secretion of mucus in the respiratory tract. Oxygen inhalations were beneficial in one of the cases. Schede gave potassium iodide to the boy who recovered, and he thinks it should be tried in every such case. He used it because of Schneidemühl's report that it relieves a certain paralytic condition in cattle.

Schede states that the *Bacillus botulinus* finds conditions favorable for proliferation not only in ham and sausage but in also canned beans, herrings and other similar foods. He advises cooking all canned beans, etc., before they are used.

TRICHINOSIS.

Review of Literature and Report of Cases. A brief review of the literature on this subject and personal observations made of fifteen patients suffering with infection by the parasite are presented by W. T. Cummins and G. R. Carson² of San Francisco.

An account of having eaten pork was given by eleven of the patients. The observations made form the basis for the following statements:

The average incubation period was three weeks. One-third of the cases presented no orbital edema; three-quarters, no eruption; four-fifths, no bronchitis; none showed splenic enlargement. Eleven cases showed a disproportionately low pulse rate, to which little attention has been called. The maximum eosinophilia was 75 per cent. Of nine cases, eight showed trichinae in the muscles; of

(2) Jour. Amer. Med. Ass'n., Sept. 9, 1916.

the fifteen cases, none were found in the blood or feces; of twelve cases, one showed an embryo in the cerebrospinal fluid; of eleven cases, none were found in the urine; of fourteen cases, ten showed albumin in the urine. The mortality was 6.6 per cent. The fatal case presented a hypostatic pneumonia and a large pleural effusion.

Evidently the parasites traverse the venous channels in very small numbers for mechanical reasons, and probably none in some cases. It would appear that in many cases they suffer partial or complete disintegration in the intestinal tract. A routine spinal fluid examination may show that the nervous tissues are invaded in many instances; but it does not seem likely that this will serve as a useful diagnostic procedure in the study of the disease. If routine urinary examinations are made for parasites, it seems not improbable that invasion of this tract may be demonstrated.

Report of One Case of Trichinosis. A single instance of marked trichinosis is recorded by Morris Flexner,¹ of St. Louis.

The patient, a white male, aged 24, was admitted to the medical service at Barnes Hospital, complaining of the swelling of the eyes, pain in the lumbar region, and fever. Family history and past history were unimportant. Illness was of five days' duration with headache and malaise. The eyes were swollen, on the second day painful and sensitive to light. He had fever and chills, his temperature being as high as 104° F.

The positive physical findings on examination were:

Edema of both eyes, with diffuse conjunctivitis, a few scattered râles in the chest, and a soft systolic blow at the cardiac apex.

Important in the blood examination was the presence of 23.5 per cent. eosinophiles.

Because of the edema of the eyes and eosinophilia trichinosis was suspected and, on questioning, the patient admitted having eaten raw hamburger steak from twelve to fifteen days before admission. He had had an intestinal disturbance.

Blood examination was carried out according to Staubil's method, that is: 10 c.c. of blood were added

(1) Jour. Mo. State Med. Ass'n., March, 1916.

to 3 per cent. acetic acid; this was centrifuged and the sediment examined with a low power microscope, using a mechanical stage; three embryos were found in all.

Flexner says that in 1905 Staubil first obtained embryos from the blood of guinea-pigs, using this method. In 1909 Herrick and Janeway first recovered the embryo of *Trichina spiralis* from the human blood. In 1910 Mercur and Baroch, Packard, Cross and Lamb all reported the recovery of embryos from the blood.

Report of Three Cases of Trichinosis. A report of three sporadic cases of trichinosis in St. Louis is made by L. H. Hemplemann.² He gives a brief history of the discovery of the causative agent of the disease, discusses its symptomatology, diagnosis, prophylaxis and prognosis. The symptoms presented by three patients referred to in this work were, severe diarrhea, nausea, severe pain in the abdomen, moderate fever, pain and stiffness in the voluntary muscles, swelling about the eyes and face, and weakness. By physical examination some stiffness and firmness of the muscles were found. A moderate fever was present in each case, and the percentage of eosinophiles found by examining stained blood-smears varied from 38 to 63. One of these patients died as a result of the disease.

The appearance of these three sporadic cases in the author's private practice during the last two years leads him to believe that the condition is not uncommon in the vicinity of St. Louis, and that the possibility of the presence of this condition must be considered in all instances of obscure febrile disease.

Epidemic of Fourteen Cases of Trichinosis with Cures by Special Serum. In view of the amount of material with which he had to work and the importance of the observations made, the statements of Benjamin F. Salzer,³ of Far Rockaway, N. Y., concerning an epidemic consisting of fourteen cases of trichinosis are quoted as they appear in the original article:

The Kernig reaction was present in all the cases.

Edema of the face occurred in all the cases.

Edema of the lower extremities occurred in six cases.

(2) Jour. Mo. State Med. Ass'n., March, 1917.

(3) Jour. Amer. Med. Ass'n., Aug. 19, 1916.

The reflexes in the lower extremities were abolished in all the cases and are still absent now (six months having elapsed since the cases first came under observation).

Trichinae were found in the blood in nine cases of the fourteen.

Trichinae were readily found in the cerebrospinal fluid in eight of the fourteen cases.

The diazo reaction was in direct proportion to the degree of eosinophilia.

Gangrene of one lower extremity was observed once.

The leukocytosis diminished as the eosinophilia increased. The blood coagulation time is markedly prolonged in trichinosis.

In one case trichinae were still found in the cerebrospinal fluid of a child 3 years of age three months after clinical recovery.

Trichinae were found in a pleural exudation once.

Trichinae were not found in the urine in any case.

Trichinae were not found in the uterus but were abundantly present in the placenta.

Trichinae were present in large numbers in the milk of a nursing woman and were found in the piece of excised mammary gland.

In one case complicated by furunculosis, trichinae were found in the pus of a furuncle of the external auditory canal. On inoculation into a rabbit, trichinosis was produced.

In two cases the duodenal tube was passed under control of the fluoroscope. In one of the two cases trichinae were abundantly found. This patient is now suffering from cholecystitis.

The feces were clay-colored throughout the disease in every case, and have the same appearance in the five cases that have remained under observation. From experimental studies it appears probable that the color is due to the reduction of bilirubin by living trichinae.

In a cat which accidentally developed trichinosis after eating a rabbit in which trichinosis had been experimentally produced, the stools were also found to be clay-colored.

Trichinae were present in the stools in all the cases throughout the disease and in three cases in which studies

in this direction were carried on after recovery. They are easily proved to be present by making the stools alkaline and allowing them to stand from twelve to twenty-four hours.

Trichinosis was produced by the injection of pleural fluid from a case of trichinosis.

Trichinosis was produced by feeding feces from cases of trichinosis to two dogs.

On feeding infected meat to animals the eosinophils appear usually within the first five days. In one case 10 per cent. of eosinophils were found after thirty-six hours. There was no leukocytosis when the eosinophilia first appeared.

The blood of a series of infected animals was examined for trichinae. After five days' examination it was negative in all. The first trichinae were found on the seventh day, two or three then being seen in each field. The temperature during the first five days remained from 100° to 101° F.

Trichinae were absent in the heart muscle, as was also the eosinophilia. Feeding of heart muscle to animals gave negative results.

Intraperitoneal injection of urine from cases of trichinosis caused no infection.

Trichinae occurred abundantly in the brain, and on injection of such tissue into animals the disease can be produced, the eosinophilia being more marked than any other form of production of the disease.

Trichinae were found abundantly in the pancreas.

As many as four coiled trichinae were found in muscle fibers.

Ascites occurred in the experimental disease in animals.

The use of serum from human patients who recovered removed the eosinophilia persisting after recovery in man or animals within forty-eight hours.

The injection of normal serum had no therapeutic value in trichinosis in man or animals. The same is true of salvarsanized serum and salt solution.

In animals the injection of convalescent serum gives an almost complete prophylactic result. Animals fed with infected meat within twenty-four hours after the

administration of the serum may develop a mild form of trichinosis. Animals fed at a period later than that prove to be immune. All these experiments were controlled.

If immune serum is mixed with infected meat and then fed, the animals do not develop trichinosis, although the ingestion of the same meat without the serum is invariably followed by the appearance of the disease.

In two cases of trichinosis in the very active stage of the disease the use of immune serum proved to be of remarkable curative value. There was a decided drop in the temperature within six hours and the abnormal temperature was entirely gone within forty-eight hours. The eosinophilia showed a considerable drop within six hours; there was then a secondary rise and then a return to the figures found in normal blood within forty-eight hours.

In twenty-four rabbits suffering from the disease experimentally produced, the immune serum had a curative effect within twenty-four hours.

Isolation of the *Trichina Spiralis*. An attempt has been made by William Lintz⁴ to determine whether or not *Trichina spiralis* can be isolated from the feces of patients infected with trichinosis. The work consisted of taking muscle tissue from autopsy on a human and feeding this tissue, which contained a large number of live trichinae, to white rats which weighed between 100 and 150 grams. The amount of muscle fed to each animal was between 4 and 8 grams. The method employed in searching for trichinae was to make a saline emulsion of the fresh feces upon a slide and examine with the low and high powered lens of the microscope. It was said that the rats as a rule became very sick within from ten to twenty minutes after feeding. They would not move around, although they were very lively previous to feeding, their heads would droop, they refused nourishment, the breathing became very rapid, and they would begin to waste away. These symptoms lasted about four days when the rats began to recover, and in two or three days appeared apparently normal. The conclusions arrived at after this work was finished were

(4) Med. Record, Dec. 2, 1916.

that at no time were trichinae found in the feces of the rat. Upon autopsy trichinae were found in the small intestines, but none were found in the large bowel or in the feces. It is thought that the trichinae evidently undergo destruction in the fecal mass. Therefore to judge by the experiment on rats, the finding of trichinae in the feces is a myth and the feces play no rôle in the spread of this disease. A warning is given that one must not confuse the various parasites found in the feces which bear some resemblance morphologically to *Trichinae spiralis*. At the autopsy from which the material was obtained for this work numerous trichinae were found in the muscle tissue, while none were found in the liver. From this it would appear that the explanation given by some, that the reason why trichinae seek muscle is because they need glycogen is insufficient, because if this were so, one certainly would expect to find numerous trichinae in the liver. The cerebrospinal fluid removed from the body at this autopsy contained a moderate number of trichinae.

Thymol in Trichinosis. In a note on thymol treatment of trichinosis, Max Kahn,⁵ of Pittsburgh, states that the second stage of trichinosis infection is difficult of treatment because the parasite has left the intestinal canal and has lodged itself in the muscles and other tissues of the body where it is difficult to reach by means of remedies administered by mouth. It is futile to give thymol by mouth after the parasite has wandered out of the alimentary canal. The thymol does not circulate in the blood as such after its absorption from the alimentary mucous membrane. From the success which the author has obtained in his work at the Western Pennsylvania Hospital, Pittsburgh, he suggests the following method of procedure:

Fifty grains of thymol are dissolved in 50 c.c. of sterile olive oil which has been autoclaved for several minutes. The solution is then resterilized and used. The patient is given from 2 to 3 c.c. of this solution subcutaneously or intramuscularly daily for seven days. The urine is examined daily for evidence of any kidney irritation, in which case the administration of thymol

(5) New York Med. Jour., June 16, 1917.

should be stopped or the dose reduced for a few days. After a week's treatment, the administration should be discontinued for about a week or ten days, and then a week's treatment should be again instituted.

The pain in the muscles, the edema of the eyelids and face, the dull mentality of the patient, all due to the parasitic influence, are very quickly relieved by this treatment. With the destruction of the parasite in the tissues it will be observed that the eosinophiles in the blood become very much increased, and the sections of the muscles will show destructive processes around and in the parasite. It has been observed that after thymol administration, showers of leukocytes appear in the urine, which upon staining were proved to be mostly eosinophiles. Before the thymol treatment, however, this was not observed in the same cases. It is thought that it may be advisable to try this method of treatment in cases of cysticercus, filaria, and echinococcus invasions of the tissue.

Neosalvarsan in Trichinosis. The results of the treatment of one patient suffering with trichinosis are recorded by J. B. McNerthney and William B. McNerthney,⁶ of Tacoma, Washington.

The patient, a man 33 years old, whose occupation was watchman for a cold storage plant, had eaten for some days undercooked ham. He became ill and continued to get worse up to the time that he came into the care of the authors. It was in his fifteenth week of disease and the patient was greatly emaciated, severely prostrated, had lost 60 pounds of weight. The temperature was 100° F. at this time. His muscles were in such condition that he could not use many of them, particularly the muscles of the arm.

The authors state that fortunately for the patient they were unaware of the use and results of neosalvarsan in trichinosis, as reported by Van Cott and Lintz. Independently they realized their utter helplessness with the usual therapy, and decided to use intravenously 0.06 gm. of neosalvarsan. During its administration the man became slightly cyanosed and it was followed by a marked chill. Within 48 hours the patient felt less pain than

(6) Jour. Amer. Med. Ass'n., Oct. 7, 1916.

for months previously, and was soon able partially to extend his forearms. Within one week he was in a chair and able to sit in an automobile, and left the hospital about ten days after he had entered. Fourteen days after the first intravenous injection he was able to walk with crutches, and three weeks later he discarded the crutches and went on to an uninterrupted recovery. During the time between admission and treatment a piece of biceps muscle contained large numbers of trichinae.

The authors state that while the work of Van Cott and Lintz would make them hesitate to use neosalvarsan, that in their own case they were rewarded with most favorable results, which seems to prove beyond a doubt that in certain stages of the disease, at least, neosalvarsan intravenously is a rational method of treatment of trichinosis.

DISEASES OF THE LIVER AND GALL-BLADDER.

Diagnosis of Functional Disease of the Liver. In a series of ninety-eight patients suffering from a variety of diseases, including twenty cases of disease of the liver, H. L. McNeil,¹ of Galveston, Texas, found seven patients with an increased amount of blood ammonia. He considered as an increase any amount over 3 mg. per 100 c.c. of blood. One of these individuals was a woman with eclampsia, whose liver at necropsy showed extensive degeneration. Another was a patient with syphilis of the liver in a fairly advanced stage; four of the patients had long-standing chronic, passive congestion of the liver from chronic cardio-nephropathy, and one was a chronic alcoholic, suffering from periodic and persistent vomiting.

In four of these cases, acidosis was present, but in the three others, including the last case, no acidosis was present.

Twenty-four other cases of acidosis, many of the severest type, studied with this point in view, showed a uniform absence of appreciable increase of ammonia in

(1) Texas State Jour. Med., July, 1917.

the blood. Also, five other cases of atrophic cirrhosis of the liver failed to show any increase in ammonia above 5 mg. per 100 c.c. of blood. As a result of these investigations, it would seem, says McNeil, that acidosis, *per se*, does not cause any excessive increase of ammonia in the blood (over 3 mg. per 100 c.c.), but that such an increase is indicative of disturbance of the functional capacity of the liver.

Case of Hepatic Distomiasis. W. de Vézeaux de Lavergue² reports a case of liver fluke diagnosed during life by microscopic examination of stools. The case was that of a soldier sent to the field hospital for "febrile lumbago" with some slight gastro-intestinal symptoms (faulty digestion, tympanites, constipation, irregular appetite, vague pains in the region of the liver, etc.).

This is the first case of distomiasis observed among French troops since the beginning of the campaign. Its interest resides in the following facts:

Diagnosis was possible during life by finding the eggs of the parasite in the feces, in spite of the insignificance of the symptoms, and because the author makes it a matter of routine to examine the stools microscopically in patients with poorly defined gastro-intestinal symptoms.

Noteworthy is the long duration of the disease—eight years with alternate periods of recrudescence and quiet; the recrudescences being considered by the patient and his friends to be a common gastritis. During one of the attacks there occurred a pleurisy at the right base. The general health of the patient was satisfactory enough to have him enlisted in the infantry in 1915 and to serve in the trenches for over a year.

The carrier of this fluke is 32 years old and a quarryman by trade, from Southern France, near the Pyrenees. It may be surmised that this is not an isolated case, and that systematic search may discover in the same region others infected with the same species of parasite.

This is a noteworthy point to keep in mind for hygiene of the central Pyrenees region.

Relation of Alcohol to Cirrhosis of the Liver. In an article dealing with the human and animal liver after

(2) Paris Med. Soc., Dec. 15, 1916.

alcohol, Frank A. McJunkin,³ Milwaukee, gives by way of introduction a brief history of cirrhosis of the liver. He says that owing to the frequent history of alcoholism, ethyl alcohol was looked on as an active factor in the production of liver cirrhosis shortly after the observations of Laennec. Later, cirrhotic livers were found in infants and youths who had never used alcohol. This confused matters until the mechanical, syphilitic, and infectious varieties were clearly defined. Now, as during the earlier observations, a feature of unknown etiology is the excessive use of alcohol, especially of distilled liquor.

In a series of thirty cases of cirrhosis of unknown etiology, coming to necropsy from the wards of the Boston City Hospital, the clinical records of twenty-eight make note of alcoholism. On the other hand a majority of those dying from chronic alcoholism in the alcoholic wards of the hospitals show no abnormal changes in the liver. The excessive use of alcohol does not, therefore, always produce liver lesions in the human being, while some workers along this line are willing to say that it never does.

The common observation was that the livers of those individuals dying from acute and chronic alcoholism show, in the great majority of cases, no change, except an abundance of fat in the liver cells. It is found true in the study of necropsies performed at the Boston City Hospital on those dying from alcoholism during fifteen years previous to 1915.

There is no question that alcohol as used by chronic alcoholics produces no liver lesion in the great majority of cases.

Out of one list of thirty workers who gave ethyl alcohol to animals, seventeen produced no lesions in the liver, while thirteen produced a cirrhosis. Those who produced cirrhosis worked with rabbits. These animals show an increase in round cells in the periportal tissue and along the interlobular lines. In this way islands of liver cells and liver lobules become surrounded by fibroblastic tissue.

In experimental work carried out by the author, alco-

(3) Archiv. Int. Med., May 15, 1917.

hol, being the most obvious factor recorded in the literature, was given persistently to animals until it was found that no lesion however slight could be produced. Later other substances were tried. A total of 300 animals were used in these experiments. Of these animals, 125 were given ethyl alcohol.

In a summary of this work, the author says:

After the elimination of cases of cirrhosis of known etiology of the mechanical, infectious, and syphilitic varieties, many cases fall into a class of unknown etiology. These cases appear to be of toxic origin, but differ from the central scleroses produced by unknown bacterial toxins and by chloroform, as well as from the cirrhosis that may follow acute yellow atrophy. Alcohol is suggested as the causative agent by the history of these cases, but there is no further evidence to indicate that it injures the liver. On the other hand the frequently mentioned fact that the percentage of cirrhosis among those dying from chronic alcoholism is only slightly greater than it is among those dying from all other cause, indicates that this substance has no direct action on the liver.

A point brought out in the histologic study of a series of human cases is that there is a very active and characteristic degeneration and necrosis of liver cells present even as long as a month after the patient received his last alcohol.

A further reason for thinking that alcohol does not act directly on the liver to produce a cirrhosis is that it does not injure the liver in the lower animals. It not only does not produce a cirrhosis, but it produces no noteworthy lesion whatsoever of the liver cells.

If alcohol does no damage to the liver, or does so only indirectly, the question of the number of factors at work in the production of these cases of cirrhosis of unknown etiology arises along with the problem of the nature of the hepatic poison. In regard to the first of these questions, the uniformity of the cellular changes, especially the characteristic hyaline degeneration of the hepatic cells, and the very irregular cutting up of the lobules and islands by rather narrow sclerotic bands, point to a single causative agent or to poisons acting alike.

As to the nature of the poison, there is little evidence now at hand. Of a number of substances given to animals, lead is the only one that produces a hyaline change. The failure of the hyalin of human liver to react with an alkaline sulphide, as does that produced by react with an alkaline sulphid, as does that produced by the active agent in this variety of cirrhosis. The uniformity of the lesion in these cases, as brought out in this study, at least tends to show that there is here a variety of cirrhosis, the etiology of which is for future solution. The so-called alcoholic cirrhosis is not produced directly by ethyl alcohol, that is, the liver is not injured by the alcohol carried to it through the blood or lymph.

[Such an article, with conclusions so much at variance with universal medical experience for a century or more, should be given little credence until substantiated by a large literature. Coming at this time when alcohol is meeting with so many rebuffs throughout the world, it is open to the unkind suspicion of being written by a partisan of alcohol or by one of those individuals who habitually take the wrong side of a controversy. It is enough here to point out that we shall go on using the term alcoholic cirrhosis of the liver just as we did before this article was written.—GEN. ED.]

Differential Diagnosis of Atrophic Hepatic Cirrhosis and Gastric Cancer without Palpable Tumor. A. E. Austin^s of Boston says that at first thought one would say that there are marked and emphatic differences between these two conditions, but that they actually are most confusing at times even after careful and painstaking investigation.

True cirrhosis occurs largely in the third and fourth decades, but we are constantly discovering cancer in the earlier periods of life. Austin has seen cancer in a young man of 28 and in a woman of 38. It has been found that habits do not play the important part formerly assigned to them, while unquestionably alcohol, he asserts, is responsible for a large share of cirrhosis, some observers say as high as 90 per cent. Yet there are many cases of cirrhosis in which strong spirituous liquors have never been used and in which the cirrhosis must be

(8) Medicine and Surg., July, 1917.

attributed to that vague, ill-defined condition known as auto-intoxication. The persistent use of strong liquors, especially cocktails, on an empty stomach is proving of importance in the etiology of ulcer, especially the malignant variety.

In the early manifestations of both cancer and cirrhosis, there is a marked similarity in the eructations, distress, if not pain, after food, constipation and loss of flesh and the frequent tendency to vomiting. So important a feature is constipation, when occurring in people toward the age of 50, after a lifetime of regular, daily movements, that some authors advise at once, a thorough examination of the gastro-intestinal functions in order to exclude early cancer.

No one has yet been able to determine accurately, just when a malignant growth of the stomach begins. The vomiting, which is common to both, differs to a certain extent in cancer and cirrhosis. In the former, it is much more liable to occur after food; at the height of digestion or possibly, once a day, particularly when there is stenosis of the pylorus, when large quantities of fermenting material are thrown off. Early morning vomiting is much more characteristic of cirrhosis, and frequently nothing but a mass of frothy mucus is ejected, much like the so-called waterbrash.

In pure cirrhosis, pain is not a prominent feature, but a feeling of distress and discomfort occurs directly after food is taken, and while this may also occur in the early stages of cancer, and may never be present when the pylorus remains patent, still, we look to pain often, as a means of clearing up the confusion between the two processes.

The emaciation of cancer is usually the outcome of the poisoning of the protein constituents of the body by its peculiar toxins, while that of cirrhosis is much more liable to be due to the utter distaste for food and its consequent avoidance than to any inherent process of the disease itself. While it is possible for short periods to maintain the weight of the sufferer from malignant disease, it is not possible to increase it; on the contrary, under favorable circumstances, that is, increase of appe-

tite and improved digestion, we can cause the cirrhotic patient to put on weight. Then, too, the emaciation of cancer is much more rapid on account of the swifter progress of the disease than that of cirrhosis, which often continues for from three to five years before the fatal termination.

Pyrosis or heartburn is common to both, but much more persistent in cancer and coming later after meals. In both, it is apparently due to fermentation and is often accompanied by eructation, but in cirrhosis there is never found the foul-smelling, putrid ructus of cancer.

Cachexia is common to both diseases and after the jaundice stage or hypertrophic cirrhosis is passed, a manifestation which does not always precede the atrophic, there is very little in the lemon tinge of the countenance in either which would enable one to differentiate these two diseases. Then, too, gastric cancer, if at the pylorus, rarely fails to exert some pressure on the common bile-duct and the mild jaundice of the Hanot form is simulated. Even if no actual superficial evidence of jaundice is found in the skin and sclera, minute traces of bile will be found in the urine.

Edema, while much more persistent in atrophic cirrhosis and often associated with extensive anasarca, is still a pretty constant accompaniment of gastric cancer, from pressure exerted by the involved glands, and can usually be elicited over the sacrum and malleoli.

As to palpatory findings, the stomach with cancer of the lesser curvature or the so-called medullary form is fully as elusive from contraction as a small atrophic liver, both withdrawing under the protection of the costal arches.

Occult hemorrhage is another factor on which we rely largely for diagnosis in early gastric cancer and rarely are we disappointed if it is persistently present with other findings. But here, again, on account of the passive congestion or circulatory stasis accompanying cirrhosis, small veins frequently rupture, producing digested blood in the feces, whereby its pathognomonic value in diagnosis of the former is much impaired. There have come to Austin's observation instances of

hematemesis with hepatic cirrhosis, which were fully as copious and frequent as in cancer.

As a general thing, however, the blood vomited in the stasis of cirrhosis is much more liable to be bright red as in ulcer, and not of the "coffee ground" variety of cancer.

The influence of cirrhosis on the stomach in producing gastritis, with loss of free hydrochloric acid and excessive mucus, is so well known that it does not demand repetition. But on this very factor, loss of free hydrochloric acid, we have long depended for aid in diagnosis of gastric cancer. It is probably true that on the incentive of increased stimulation by food, which tends to exaggerate secretion, the stomach of gastritis responds better than that of malignancy; but the margin is so narrow that not much dependence can be placed upon it.

Stasis is a finding on which is placed much dependence for the diagnosis of gastric cancer, when located at the pylorus, but when in the walls elsewhere, or at the lesser curvature, the retention is so slight that it is discoverable as a general thing only by the radiologist. In a case of hepatic cirrhosis, in a man of 82, accompanied by high acid values of the gastric content, stasis was so great that repeated lavage was necessary to relieve him, and he is still living, two years later.

To illustrate his points Austin cites the histories of two cases—one of cirrhosis and one of cancer. He concludes his article with the following summary:

Moderate but persistent use of alcohol may cause gastric ulcer and subsequent cancer, as well as hepatic cirrhosis, though much less frequently, or both may occur without the action of alcohol.

Age has not the importance formerly attributed to it in the differentiation of these two conditions.

Symptoms, such as eructation, vomiting, heartburn, distress after food and moderate pain, may be common to both.

Physical signs, such as cachexia, emaciation, ascites, hematemesis and gastric stasis may occur with both diseases.

Gastritis with suppression of free hydrochloric acid and occult blood in the feces, as well as urobilinuria and

bilinuria, are found in both gastric cancer and hepatic cirrhosis.

Echinococcus Cyst of the Liver. The occurrence of a single cyst of this kind in the left lobe of the liver and discharge of the cyst into the left hepatic duct is described by Russell S. Fowler.³

He states that echinococcus cyst involving the biliary passages, upon which operation has been done and rupture of such cysts into the biliary passages, is very uncommon. In discussing the condition, he states that rupture causes sudden blockade of the common duct and is the occasion of very severe biliary colic. There is profound collapse, and death has been known to follow immediately. Frequently the condition is diagnosed as calculus obstruction. A correct diagnosis is only possible if echinococcus elements are found in the stool. In cases in which the cyst does not present as a tumor, the differential diagnosis is between liver abscess, cholangitis with chronic stone, or a tumor blocking the common duct; the diagnosis is only possible when cyst elements are recognized in the feces. Occasionally, rupture occurs without symptoms; then also the condition can only be recognized by the appearance of echinococcus elements in the stools. In some cases there has been rupture into the veins of the liver or inferior vena cava followed by the carrying of embolic cyst elements to the heart and pulmonary arteries occasioning immediate death. The usual symptoms of rupture of such a cyst into the biliary passages are severe pain, chills and fever. The obstruction in the common duct accompanying the rupture may be by impaction of cyst contents or by inflammatory swelling caused by the intense irritation.

The details are given of a single case in which a cyst of the left lobe ruptured into the left hepatic duct and resulted in extensive inflammatory reaction in the common duct and the gall-bladder with subsequent acute dilatation of the common duct. The treatment consisted of drainage of the gall-bladder and finally of the common duct and placing a catheter through the common duct into the left hepatic with subsequent irrigation of this part of the bile passages. Echinococcus elements

(3) *Archiv. Diag.*, July, 1916.

were not found in the feces at any time during the course of the disease in this patient. The detritus removed at operation showed everywhere echinococcus cyst wall and hooklets. Characteristic hooklets were found in the detritus passed through the common duct tube post-operatively. The result appeared to be a complete cure.

Echinococcus Disease. L. Davis and G. M. Balboni* of Boston report that in the last three years the echinococcus complemental test has been used at the Massachusetts General Hospital. Ninety-seven tests in all have been made. Twelve were positive and eighty-five were negative. Of the twelve positive cases, seven proved to be echinococcus disease. One of the five other patients at operation showed an abscess in the abdominal wall, which on microscopic examination showed no evidence of tuberculosis. Its appearance was not consistent with echinococcus cyst. One patient had clinically a large spleen and liver, a positive Wassermann reaction, and was not operated on. Three patients were clinically syphilitic and had weak to strongly positive Wassermann reactions. Among the eighty-five negative cases, twenty-four had a positive Wassermann reaction. The Wassermann reaction was negative in five of the proved echinococcus infections. It was not done in the remaining two. There was some variation in the strength of the echinococcus reaction in the same patient from time to time. The cyst fluid proved a better antigen than the alcoholic extract of the cyst wall. The cyst fluid was found active as an antigen after more than eighteen months outside of the body. The cysts were located in the liver alone in sixteen; in five cases other parts as well as the liver were involved, namely, peritoneal cavity twice, omentum lung and kidney once each. In the other eight cases the cysts were found in the brain, heart and pericardium once, kidney twice, peritoneum once, gastrohepatic omentum once, and retroperitoneum twice. In one case echinococcus cysts were passed in the feces, in another case they were passed with the urine.

(4) Boston Med. and Surg. Jour., May 24, 1917.

Hepatic Abscess Mistaken for Cancer. In this case, reported by E. Ordiozola,⁵ a young man of 27 consulted him with symptoms which he decided indicated cancer of the liver. The patient died and autopsy showed a large abscess on the posterior surface of the liver.

The author states that suppurative processes in the liver should be excluded before any other condition is considered. Abscesses are most frequently mistaken for other diseases. There may not be any trace of jaundice and absence of gastro-intestinal disturbances is by no means uncommon. Pain in the shoulder occurs early in the disease; it is acute and persistent. Exploratory puncture is advised by Ordiozola, as this will usually clear up the diagnosis. The blood picture he states is not characteristic. When abscess is suspected operation is imperative.

Amebic Abscess of the Liver. An account of the occurrence of this condition in a single patient, a soldier, 27 years old, is given by H. L. Watson Wemyss,⁶ medical officer in the British Army.

Two weeks after the patient landed in Gallipoli, in August 1915, he suffered from severe diarrhea which continued for six months. Two months after the outset he received two injections of emetine which gave temporary relief. Three months after the outset he suffered with pain in the upper part of the abdomen, he became jaundiced and the diarrhea persisted. His blood then gave a strongly positive Widal reaction, which was confusing however, due to recent inoculation with typhoid vaccine. Cultures of the blood, the urine and the feces did not reveal typhoid bacilli. There was more or less constant fever, especially in the afternoon and evening, and a progressive loss of weight to the extent of more than 14 pounds.

Seven months after the outset, the man's temperature was as much as 101° F. at night and he complained of pain on the right side over the liver. Friction was heard at this time over a small area just above the costal margin in the right mid-clavicular line. The leukocyte count rose to as high as 28,000 per cubic millimeter, 80

(5) *Cronica med.*, June, 1917.

(6) *Edinburgh Med. Jour.*, October, 1916.

per cent. of these being polymorphonuclears. The red count was 3,500,000 per cubic millimeter. There was much embarrassment of respiration, a great increase in the vertical diameter of the liver and a definite lowering of the general condition of the patient. The last of three exploratory examinations with a large needle and syringe resulted in the removal of chocolate-colored fluid through the seventh interspace in the posterior axillary line; following this, the eighth rib was resected and four pints of chocolate-colored material removed from this region.

Repeated examinations, bacteriologic and microscopic, of the material removed failed to reveal amebas. Neither were the organisms found in tissues removed at the time of the operation. Emetine was administered following which the size of the liver rapidly receded and the condition of the patient improved.

The chief interest in the case is from the diagnostic standpoint which shows how the diagnosis of typhoid fever and such affections of the liver may easily be confused and how the fixation of the idea that one disease is present may lead to entire neglect of other possible conditions.

Effect of Methyl Salicylate on Production of Bile. This experimental study has been made by G. Leone.⁷ The point which appears to have been established is that this drug has the power to increase materially the amount of bile secreted and of its total solid residue. Soon after ingestion or subcutaneous injection of the drug the bile becomes more fluid, but the osmotic tension and the electric conductivity are higher as the total dry residue and ash increase. Six series of experiments at intervals of one or two months were made on guinea-pigs, kept all the time on a constant diet and showing no change in weight. The bile output increased much more, proportionately, after a dose of 1 gm. than after a quarter of this dose.

Disturbance of the Law of Contrary Innervation as a Pathogenetic Factor in Diseases of the Bile-Ducts and the Gall-Bladder is the title of an article by S. J.

(7) *Riforma Med.*, Vol. 32, No. 1.

Meltzer,⁸ working in the Department of Physiology and Pharmacology of the Rockefeller Institution for Medical Research.

He states first that the gall-bladder has a definite place in the physiologic organization of the animal body. Like the urinary bladder it presents an ingenious but simple mechanical device by means of which a continuous glandular secretion is transformed into a discontinuous elimination. The following are some of the facts which are proof that such an arrangement is beneficial: In the first place it is known that bile salts, as well as bile pigment, may be absorbed from the intestines to be stored up again in the gall-bladder. Bile in the intestines at a time when it is not needed for a specific digestive action is liable to exert some injurious influence. Bile in the gall-bladder is a great deal more concentrated than that which is present in the system of biliary ducts. When, therefore, the intestinal digestion is in that state which requires the activity of the bile it is received by the aid of the gall-bladder at once in a concentrated form. While these facts indicate that the storing up in the gall-bladder is a physiologic and advantageous process, it also shows the possibility of the pathologic element of stasis. Bile even under normal conditions contains often living pathogenic organisms. They may be brought there in various ways as directly from the duodenum, due to portal blood or by being eliminated by the general circulation. Two elements are of importance in preventing the development of the inflammatory processes of the biliary system, though even the bile contains living pathogenic organisms. One is the maintenance of normal vitality of the mucous membranes of the gall-bladder and the bile ducts; microorganisms prefer to settle and grow on tissues which have lost their resistance. The other safeguarding factor is the absence of an abnormally prolonged stasis of the bile in the various parts of the biliary system. Bile stasis is of primary importance as a pathogenic factor in biliary diseases. Meltzer asks whether or not conditions happen which are capable of converting the periodically occurring physiologic quiescence of the gall-bladder into an abnormally prolonged

(8) Amer. Jour. Med. Sci., April, 1917.

quiescence and thus converting the physiologic storage of the bile into a pathologic stasis. He also asks: What is the nature of the mechanism which in normal conditions causes the stream of bile at one time to be emptied into the duodenum, and at another time to be diverted into the gall-bladder?

Here a new phase of the subject is taken up. It is said that the law of contrary innervation is manifest in all functions of the animal body, and it is the author's belief that a disturbance of this law is a factor of more or less importance in the pathogenesis of many disorders and diseases of the animal body. Many years ago he called attention to the general principle that impulses inhibiting the action of antagonists must be an integral part of any kind of a movement in the animal body. For instance, simultaneously with each contraction of the extensors an inhibition of any form of contraction of the flexors, and *vice versa*, must take place. Otherwise normal locomotion, for instance, would be practically impossible. This same arrangement has been shown to hold true in the respiratory mechanism, in the process of deglutition, and in the so-called law of the intestines named by Bayliss and Starling. Sherrington applied the name of reciprocal innervation to the same process. Meltzer's name for this process was the "law of contrary innervation." He says again that the gall-bladder is well provided with muscle fiber, the contraction of which will free that viscus of the fluid contents.

The papilla of Vater is provided with circular muscle fibers which by their contraction close up the common duct.

Meltzer believes that it has been sufficiently established that the physiologic discontinuous character of the flow of bile into the duodenum is regulated by a reflex mechanism dominated by the law of contrary innervation; that the integrity of the gall-bladder is an important part in this reflex mechanism; that the discharge of bile can be greatly curtailed by the absence or a restriction of the discharge of chyme from the stomach into the duodenum, and that the discharge of bile through the papilla of Vater into the duodenum is greatly in-

hanced by the presence in the lumen of the latter of peptones or albumoses.

The mechanism of bile storage and of bile discharge is depending on such a fine nervous adjustment that we can readily conceive a disturbance of it without the presence of a concomitant palpable anatomic or chemical disorganization. One only need assume that by some mental excitement the tonic contraction of the sphincter of the common duct, at the period assigned for the discharge, does not become relaxed while the gall-bladder contracts within the usual normal limits; this would result in abnormal stasis within the biliary duct which might lead to icterus—emotional icterus. Besides psychic influences (perhaps disorganized internal secretions which are conducive to a disturbance of the emotional equilibrium) there are the influences of the partaking of food, and of the character of the food which may prove sooner or later to be pathogenetic factors in the formation of biliary diseases. Simple infrequent feedings, say the partaking of only one meal, or even two meals a day, may very gradually lead to pathologic consequences. The abstaining from protein or taking of protein infrequently or in minimum quantities may prove to be another factor in the pathogenesis of biliary disease.

From these considerations it follows, says Meltzer, that even in health it is advisable to take comparatively frequent meals, although they may not consist of large quantities, and that the meal shall contain food which readily sends peptone and albumoses into the duodenum. This principle ought to be especially observed in infectious diseases during which the bile contains the causative organisms. In typhoid, for instance, food should be administered every two hours, and the food should contain materials which may be readily converted into peptone and albumoses. The frequent elimination of the bacteria-laden bile may be the means of preventing the development of cholangitis and cholelithiasis. The direct administration of peptone in capsules may be useful in infectious disease as well as in some of the biliary disorders.

Prognosis in Diseases of the Gall-Bladder. In discussing this phase of disease of the gall-bladder, Henry

Wald Bettman,⁵ of Cincinnati, calls attention to the different viewpoints obtained by the practitioner, the gastro-enterologist and the surgeon because of the different stages at which patients are seen by these different men. There follows some discussion of the symptoms and etiology of gall-bladder disease. The author says that many facts are available to show that a healthy gall-bladder has considerable resistance to disease; that a once inflamed gall-bladder may become restored to normal conditions is proved by many operations undertaken after one or more attacks, but which reveal the gall-bladder to be again sound. That the healthy gall-bladder of dogs has the power to dissolve human gall-stones, Bettman says, has been repeatedly demonstrated by experiments.

The author considers that it should constantly be borne in mind that the formation of gall-stones is a slow process, taking place insidiously during many months, in a chronically inflamed gall-bladder, in which colon or typhoid bacilli are thriving. The impression is given that it is not too optimistic to believe that under certain conditions the bacterial activity in the bile can be favorably influenced; that the resistance of the gall-bladder to the deposit of cholesterin may be heightened by combating the inflammation present; that recently deposited detritus may even be redissolved or at least swept away and that, in fact, to a certain extent therapeutics may be said to be active in preventing the formation of gall-stones.

By use of hot packs, bed-rest, appropriate diet, the judicious administration of salines, antiseptics and mild cholagoges, the author thinks that in many cases the disease can be brought to a definite and permanent stop. However, after the disease is once firmly established and stones are deposited, such a good outcome can not be expected. Stones can not be dissolved, nor, except by rare chance, can their expulsion be effected. In other words, cholelithiasis can not be cured by any known medical means.

Concerning the influence of age on the prognosis in gall-bladder disease, this writer says that whereas the

(5) *Lancet-Clinic*, Sept. 16, 1916.

incidence of gall-stones increases with age, the morbidity diminishes after the age of 60. Numerous statistics are quoted concerning this point, and the author closes this part of the discussion by stating that general statistics on this subject are a poor guide to prognosis in any individual case.

He further states that after gall-stones are formed and after a typical gall-stone clinical history is established, whether referable to the gall-bladder or the stomach, the prognosis will depend to a large extent upon the degree of pathologic changes which have taken place in the gall-bladder and bile-passages. The lodging of a stone in the cystic duct with distention of the bladder, thickening of the wall of the bladder, the formation of adhesions between bladder and duodenum, febrile attacks, due to exacerbations of gall-bladder infection, all of these complications which can usually be recognized, point to the probable futility of further medical treatment and indicate that the patient's best chances for health and safety lie in the domain of surgery. In the absence of these complications the prognosis is an open one.

Drainage of the gall-bladder, when done for typhoid cholecystitis, is not safe, and is usually superfluous, as in nearly all cases of typhoid cholecystitis recovery ensues under medical treatment. In ordinary acute catarrhal cholecystitis it is uncalled for. When performed it does not, so far as is known, prevent recurrences or future infections.

Concerning the relation of cholelithiasis to cancer of the gall-bladder, he states that because gall-stones are present in from 70 to 90 per cent. of primary cancer of the gall-bladder, it has been assumed generally that the stones caused the cancer. This conclusion, however, obvious as it may appear, should not be accepted as a demonstrated fact. Cancer of the gall-bladder is known to develop frequently in the absence of stones. Mere attacks of biliary colic need not arouse fear of the development of cancer. On the other hand, he states that empyema or chronic ulcerative conditions which run a less acute but a more obstinate course are more apt to be followed by cancer, and for this reason justify the

conclusion formerly given by the author, that gall-bladder disorders which do not yield to medical treatment should be operated on.

Pathogenesis of Gall-Bladder Infections. The results of H. J. Nichols'⁶ experiments support the theory of descending infection of the gall-bladder through the bile from the liver. Infection of the gall-bladder wall can not be ruled out absolutely and probably occurs at times, but the bile-ducts seem to be the regular avenue of infection. This conclusion suggests, he says, that prophylactic measures and possibly curative measures should be directed toward the bile rather than toward the bloodstream and tissues. Vaccination, for example, appears to have little effect in the prevention and cure of experimental or clinical lesions, and in fact may favor the production of lesions by increased elimination of organisms in the bile. Human bile must have some antiseptic action, because, in any septicemia, some microorganisms undoubtedly pass through the bile-ducts and gall-bladder, but in only a comparatively few cases do they produce a definite cholecystitis. Alkaline therapy is suggested by Nichols in the prevention and cure of gall-bladder disease.

Gangrene of the Gall-Bladder. This case is reported by O. Cignozzi.⁷

The patient, male, aged 39, had had two attacks of gallstone colic during the last seven years. The present attack lasted forty days before the gall-bladder was removed; it began with rise in temperature and was accompanied by vomiting.

At operation, the gall-bladder was found to be gangrenous throughout; it contained 205 gallstones. The absence of adhesions indicated that the inflammatory process was not of long standing. The gall-bladder was found completely covered with omentum, which had thus prevented the escape of gallstones into the abdominal cavity.

Gastric Disturbances in Gall-Bladder Disease.⁸ In a discussion of this subject William Fitch Cheney⁹ says

(6) Jour. Exp. Med., November, 1916.

(7) Policlinico, surg. sect., 1917, No. 5.

(8) See also Diseases of Stomach, this volume, p. 157.

(9) Archiv. Diag., April, 1917.

that in sifting the meaning of "stomach troubles" three possibilities always present themselves: First, the symptoms may be due to organic disease of the stomach itself; second, they may be due to a disease elsewhere; third, they may be due to neurasthenia.

In the second group the two great factors in producing gastric disturbance are chronic appendicitis and chronic cholecystitis; there are numerous others, but these two stand out conspicuously. Each plays an important part; but both are alike in this, that no medical or dietetic treatment directed to the stomach does any permanent good until the underlying pathology is recognized and eliminated.

During the five years from Jan. 1, 1912, to Jan. 1, 1917, the author had seen sixty-two cases that belong in this second class; they had been selected from 2,116 patients who passed through the internal medicine clinic. These figures at once demonstrate that gall-bladder disease does not form a large proportion of such material. These sixty-two cases are divided into three classes: First, those without any complaint of stomach trouble between the characteristic attacks of gall-bladder disease; second, those with a mixed picture, of gall-bladder attacks at longer or shorter intervals and more or less constant stomach trouble between times; third, those with gastric disturbance predominant and gall-bladder attacks so slight, so infrequent or so conspicuous by their absence that no proof exists for a long period that the gall-bladder is the real source of the ailment.

In the first group of thirty patients, fifteen were operated upon and the pathology found as diagnosed. Cheney says that it seems reasonably clear, therefore, that when no chronic gastric disturbances exists and the history clearly points to the gall-bladder as the seat of the disease, we are not likely to err in diagnosis between the two.

In the second group there were twenty-eight cases; there was constant complaint of distress produced by food as well as intercurrent attacks of severe pain in the right hypochondrium, corresponding in description to biliary colic. Some of these patients complained of loss of appetite, distress soon after eating, a feeling of full-

ness, bloating and distention, much belching of gas, constant nausea and frequent vomiting; others made "sour stomach" the burden of their story; acidity, burning sour eructations, and pain; consciousness of their stomach at all times, no matter what they ate. Cheney declares that the danger in these cases is that the gastric history will have so impressed the patient that the attacks of biliary colic are forgotten, or suppressed in the relation of symptoms.

As regards gastric analysis, the most common finding in this group was hyperacidity. But just as there may be no stomach trouble whatever in the intervals between the attacks of biliary colic, or symptoms corresponding to gastric ulcer or chronic gastritis or gastric neurosis; so there may be found hyperacidity, subacidity, anacidity or normal gastric juice.

The most puzzling instances are those of the most persistent stomach trouble of one kind or another, really due to gall-bladder disease, in which no history can be elicited that would suggest the gall-bladder as the organ at fault. Four of the sixty-two cases studied in this series belong to the third group. After giving details of these four cases, Cheney says that they are apparently rare, but may occur oftener than is thought. After months or years of quiescence, with no manifestations but reflex ones in the stomach, the gall-bladder may produce an attack or series of attacks that make the preceding history perfectly clear; but before this time we have no certain proof as to the origin of the dyspepsia. Radiographic plates, however, seem to offer hope; either on the one hand by the elimination of such serious organic changes of the stomach as are produced by ulcer or cancer; or on the other hand by demonstrating the presence of gall-stones or of distortion of the pylorus resulting from gall-bladder adhesions. In any event, the possibility of gall-bladder disease must always be remembered in every indefinite case of stomach trouble which is inclined to come under the heading of "gastric neurosis."

[These cases of the author's third group are very difficult to diagnosticate. If, however, every case of aberrant gastric symptomatology arouses the suspicion of disease

of the gall-bladder or of the appendix errors are not so frequent as they otherwise would be. A very searching question which the physician should ask himself in such an instance is: "Am I dealing with an infection or not?" It is astonishing how frequently definite signs of infection will crop out when the patient's history is canvassed afresh or he is again examined with that question definitely in mind. Joint disturbances, occult and partially forgotten febrile attacks, septic headaches, or other evidences of infection clarify the case and make certain the diagnosis.—GEN. ED.]

Hypercholesterinemia in Cholelithiasis. Exactly as some individuals have a so-called gouty or uric acid diathesis with a retention of uric acid, M. A. Rothschild and H. Rosenthal¹⁰ hold that some individuals retain their lipoids and the result is a retention hypercholesterinemia, the excretion of a more or less saturated bile, and ultimate precipitation of the retained cholesterin in the gall-bladder, the common duct and its finer radicals.

The subsidence of an attack means that the patient has rid himself of the obstruction and will be in good health until the saturation point in the blood and bile is again reached. The recognition of this diathesis, the authors emphasize, is extremely important for the patient. Under proper dietetic management in a large percentage of these cases a secondary operation might be avoided. Hence one should examine the blood of every patient with cholelithiasis without jaundice for cholesterin before operation.

In the presence of hypercholesterinemia, provision should be made for drainage of the bile to deplete the body of the retained liquids. The drainage tube should not be removed until the blood and bile show a normal cholesterin content, and during this period the diet should be low in liquids. Further accumulation of cholesterin can be controlled by dietetic measures, placing the patient on a fat-free diet which both excludes lipoids to a large extent and renders difficult the esterization of the free cholesterin in the food.

(10) Amer. Jour. Med. Sci., September, 1916.

On a strict, practically lipoid-free diet, only vegetables are allowed by the authors. Beans and peas which are fairly rich in a metamerie product, phylocholesterin, are excluded. All other vegetables, as well as cereals and sugars, are allowed. The milk should be skimmed and fat-free buttermilk permitted. This diet is so strict that the majority of patients will not maintain it for a long period; therefore, the authors have devised "fast and feast day" periods. For three or four days a week the patient lives on the strict, lipoid-free diet outlined above, the so-called fasting periods, which serves to deplete the organism of the stored-up lipoids. For the next three or four days, dependent on the grade of the hypercholesterinemia, a more liberal diet is permitted, the so-called "feast days." On the "feast days" the patient is allowed, in addition to the articles stated above, well-cooked lean meats and fish, excluding salmon, shad and bluefish, the fat content of which is high. Oleomargarine is allowed instead of butter.

Acquired Hemolytic Jaundice. The record of a single instance of acquired hemolytic jaundice with splenectomy is presented by G. A. Friedman and Elihu Katz,¹ of New York. The patient was a man, 18 years old, who gave no family history of previous icterus or of any disorder of this nature. The chronic enlargement of the spleen, the acholuric non-obstructive jaundice not causing pruritus, the absence of bile from the urine and the presence of bilirubin in the blood serum, the positive reactions for urobilin and urobilinogen in the urine, the anemia, and the granulation of the red blood-cells with their slightly increased fragility to hypotonic salt solutions all pointed to this condition. From the fact that there was no hereditary basis for the icterus, and from the late and rather sudden onset, it was evident that the case belonged to the acquired type.

In commenting on the case the authors say that hemolytic jaundice is associated with an increased blood destruction, resulting in a somewhat characteristic blood picture and blood findings, and icterus and splenomegaly.

The cause for the hemolysis is not at all clear, but recent operative and experimental results have proved that the

(1) Jour. Amer. Med. Ass'n., Oct. 28, 1916.

spleen is an essential, if not the main factor in the etiology of the disease, but that as in other hemolytic diseases, pernicious anemia, for instance, many other factors are perhaps involved. The liver, too, probably plays an important rôle. Just how the spleen and liver act, however, is not definitely known. Vogel believes that the spleen probably acts by bringing the red blood cells more closely into contact with the pulp cells, where there is not so much blood destruction; but, perhaps, the red cells are so affected or sensitized as to render them more susceptible to hemolytic action on the way to the liver, or, more probably, to destruction by the Kupffer cells of that organ. The enormous hyperemia in the spleen sinuses, with practically no large phagocytic cells containing red blood corpuscles or blood pigment, the absence of excessive iron deposition in the organ, and evidence of marked stasis of blood with relatively little blood destruction, seem to favor this view.

Toxic Jaundice in Munition Workers. In this article Matthew J. Stewart,² of Leeds, deals with the morphologic changes in the blood occurring in a series of fourteen clinical cases of toxic jaundice from trinitrotoluene poisoning; and with certain points in the morbid anatomy of the disease as observed in a series of seven fatal cases. While only a relatively small number of cases have been dealt with for a short period of time, he says that sufficient has already been made out to show that very profound changes in the composition of the blood may occur as a result of trinitrotoluene poisoning; indeed it might be said that such changes are the rule in cases in which pronounced clinical symptoms, and especially jaundice, have manifested themselves. In considering the changes in the leukocytes, work was done on the basis of the absolute number per cubic millimeter of each variety of leukocyte and the following fairly elastic figures were taken as the limits of the normal:

Neutrophil polymorphonuclears	3600-6750 per c.mm.
Lymphocytes	1200-2700 per c.mm.
Eosinophils	30- 360 per c.mm.

The leukocytic changes as calculated on this basis are

(2) Lancet, Jan. 27, 1917.

given as: (a) neutrophil leukopenia, (b) neutrophil leukocytosis, (c) lymphocytosis and (d) eosinophilia.

The most striking of the leukocytic changes was neutrophil leukopenia, which was present at some stage of the disease in nine out of fourteen cases. In four of these nine, and two of the four fatal, the leukopenia was extreme, under 1,100 per c.m.; of the other five affected the highest neutrophil count was 3,175. In the two fatal cases the leukopenia was progressive and terminal, the final counts being 120 and 636 respectively. Stewart says that a progressive failure of the leukoblastic function of the bone-marrow is therefore to be regarded as one of the most common manifestations of the severe trinitrotoluene poisoning, but that it is not a constant feature in fatal cases is shown by certain of the records which he gives in detail in this article.

Whether a neutrophilic failure is due to a direct action of the poison on the leukoblastic tissue can not be said with certainty, inasmuch as all the cases in which it occurred presented clinical evidence of an antecedent or accompanying hepatic lesion (jaundice, etc.), while both the fatal cases showed a typical advanced trinitrotoluene cirrhosis of the liver at post-mortem examination.

In one case there was a neutrophil leukocytosis. At first the total leukocyte count was 14,200, of which 10,000 were polymorphonuclear leukocytes, and later the count was 22,000 and 19,200 (87.25 per cent.) polymorphonuclear leukocytes.

The lymphocytosis was one of the most commonly observed changes. It occurred at some time or other in nine out of fourteen cases, and varied in different patients from 3,150 to 5,100 per c.m. The chief point to be observed was that even in fatal cases and in those showing profound polymorphonuclear or erythrocytic failure the lymphocytes were maintained at or above the normal level. In two cases the lymphocytosis was the only change noted.

Eosinophilia was observed in three of these cases, and in two of these it was well marked, once accompanying a marked neutrophil leukocytosis, once with a slight neutrophilia.

Changes in the erythrocytes and hemoglobin were

much less conspicuous than the leukocytic changes. A serious degree of anemia was observed in three cases only. All the others, including two of the fatal cases, had red cell counts of over 4,000,000, but a slight grade of chlorotic anemia was present in several. In the three serious cases the anemia was of the "pernicious" type, with a color index over 1, but very varying degrees of severity were presented.

In reference to the morbid anatomy, Stewart says that one of the chief problems here was the nature of the liver changes. The lesion appeared to lie somewhere between a subacute yellow atrophy and an ordinary multilobular cirrhosis of irregular distribution. The action of the poison on the hepatic cells is thought to have been probably slow and insidious, and the degenerative changes were speedily followed, if not actually accompanied, by leukocytic infiltration and fibroblastic overgrowth. The degenerative and other processes once set going were progressive, even when the patient had been removed from the influence of the poison. In a certain proportion of the cases a fatal termination ensues in from four to twelve weeks after the first symptoms. The spleen was never appreciably enlarged, the weight varying from four to seven ounces in different cases. Ascites was present in three, and hemorrhages in various situations were present in five cases, most frequently in the peritoneum and pericardium.

Pathology, Chemical Diagnosis and Urinary Findings in Picric-Acid Jaundice. Out of 117 cases of jaundice passing under their observations, M. Bruté, M. Gairllier and B. Baeckerout³ found ten cases due to picric-acid ingestion. The diagnosis was made by finding picric acid or its derivatives in the urine. It is by this means alone that picric-acid jaundice can be distinguished from other jaundices. The statement that picric-acid jaundice is a "false jaundice" and that the coloration of the skin is due to the deposition therein of picric acid and not to biliary pigments, the authors deny. In the urine of seven of the patients an excess of urobilin was demonstrated quite commensurate with the degree of jaundice present.

(3) *Presse méd.*, Sept. 28, 1916.

In order to control the findings three experiments were made on dogs with varying doses of picric acid. The urinary findings were as follows: Biliary pigments were constantly found in the urine after investigation of the poison. Bile-salts appear first, then pigments and urobilin, showing that the jaundice was not due to obstruction of the bile-ducts, but to an actual damage to the hepatic cells.

From their observations and experiments the authors draw the following conclusions:

All jaundices from the ingestion of picric acid are true jaundices with lesions in the liver cells; they can not be distinguished from other hepatogenous jaundices by any certain clinical sign.

Chemical diagnosis is the only means of telling a picric-acid jaundice. It is based on the extraction of picric acid itself when the ingestion has been recent and considerable, and upon the extraction of picramic acid which is present a long time after ingestion. Biliary pigments, if present in the urine, do not interfere with the detection of picric acid.

The urine in picric-acid poisoning may contain biliary pigments, but in general it may be said that picric-acid jaundice is only a slight jaundice and therefore urobilin only may be found.

Infective Jaundice (Weil's Disease) in British Army.

In a preliminary report of their observations on infective jaundice (*Spirochaetosis ictero-hemorrhagica*), N. B. Gwyn and J. J. Ower,¹ Captains in the Canadian Medical Corps, described the clinical course of the cases under their observation as follows:

There is an abrupt onset with chill, or a more gradual one with intense headache, dizziness, nausea, persistent vomiting, diarrhea and abdominal pain. Fever and thirst and an intense aching of the muscles, particularly those of the legs, were complained of within a few hours. An irregular fever developed. Jaundice was noted within from 48 to 72 hours; at times it was of but slight degree, gradually deepening in the severe cases, in which perhaps a more marked biliary obstruction existed. At times hemorrhages into the conjunctiva and the skin

(1) Lancet, Sept. 16, 1916.

were observed. A decided albuminuria with numerous casts and red blood cells was a striking feature. In the severe cases, the prostration was practically a collapse, the muscular soreness preventing movement, the muscles themselves being actively inflamed and the legs swollen. Active delirium, even in the absence of high fever, was seen; drowsiness was more common, however. After three or four days, in a mild case, the fever gradually dropped, vomiting and abdominal and muscle pain subsided, diarrhea ceased, the urinary flow increased and the albuminuria quickly disappeared.

Continued vomiting, diarrhea and pain, with the signs of severe toxemia, were seen in one instance in which there was no fever.

In one fatal case the patient had a subnormal temperature for the six days during which he was under observation.

Important among the physical findings are jaundice of greater or less degree, injection of the conjunctivae, herpes, dry tongue, sordes, and late-appearing papular rashes with severe prostration. A total absence of signs or symptoms referable to the heart or lungs was noted, and contrary to the usual idea the liver and spleen were not easily felt or made out to be definitely enlarged. The abdomen was found to be tender, not as a rule distended, resistant if the pain were extreme. No localization of pain could be determined in any case.

A leukocytosis, averaging 15,000 per c.mm. was found.

The presence of typhoid and paratyphoid organisms was ruled out by blood-cultural methods and agglutination tests.

After the authors had had considerable experience in caring for patients of this type they were informed of the work of the Japanese on similar conditions, and thereafter made search for the spirochete described by the Japanese workers.² In most instances the patient had advanced too far for the organism to be found.

In one case, however, the spirochetes were found both in fresh preparations of blood and in cultures of blood. In order to avoid confusing this organism with other spirochetes the author studied those demonstrated in the

(2) Practical Medicine Series, 1917, Vol. I, pp. 148-151.

accompanying illustration (Fig. 18). The report of their results in a single instance is given in order to stimulate others to further investigation of soldiers suffering with similar conditions.



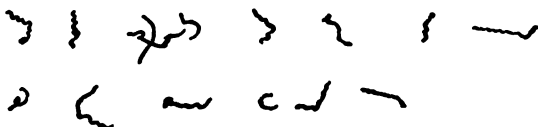
Myelin bodies from serum after 24 hours and from a hæmorrhagic pleural exudate, showing movements and various shapes assumed. Dark-field illumination. Red blood cell on the left as a standard of size.



Motile spirochetal forms seen in centrifuged serum from Case 5, and drawn at the time of observation. Red blood cell as a standard of size.



Three types of spirochæta under one observation. Fontana (silver) stain. A = *treponema pallida* (from chancre). B = *spirillum obermeieri* (from blood). C = *spirochæta ictero-hæmorrhagica* (from serum).

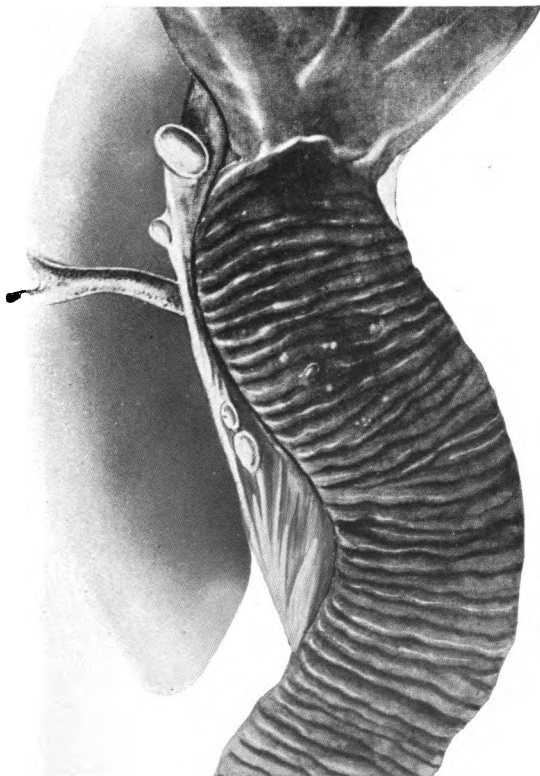


Spirochæta-like bodies in culture (three to five days). Fontana (silver) stain. $\frac{1}{4}$ inch objective.

Fig. 18.

Basing their account chiefly on a study of 178 cases of jaundice, which were admitted during nine months to the Fourteenth General Hospital, the Fourteenth Stationary Hospital in the British Service, Bertrand

PLATE VI.



The stomach and duodenum from a case of spirochaetal jaundice, showing the œdematous and congested mucous membrane and the papilla. The common bile duct shows no change. The neighboring glands are enlarged. (See page 305.)

Dawson and William Hume³ present an article on "Jaundice of Infective Origin." They classify their cases as: spirochetal jaundice, enteric jaundice and catarrhal jaundice, the last including some indeterminate forms.

Most of their cases were studied before the Japanese work was known to them, and the actual demonstration of the spirochete is lacking in many of them. More recently, however, they obtained the spirochete from the urine in a majority of patients suffering from both the severe and mild types of the disease.

The production of the disease in a guinea-pig by inoculation with a patient's blood can be effected only in the first three or four days of illness, and the cases seldom reach base hospitals at this early stage. Those cases of jaundice due to spirochetes are classed as severe and mild. Under the first group eighteen cases are considered and the symptoms are described in a general way. Fifty-eight patients with the milder type of disease are considered and the symptoms seen in them are tabulated. Since this table of symptoms contains all those included under the first group, the latter is given only.

SYNOPSIS OF FIFTY-EIGHT MILD CASES.

1. Onset—	
Gradual	42
Sudden	16
2. Initial fever	58
(Average length of fever, 6 to 8 days)	
3. Conjunctival suffusion and photophobia.....	50
4. Jaundice—	
Well-marked	51
Slight	7
5. Herpes labialis	30 (approx.)
6. Hemorrhage	Very low
(There is sometimes sputum tinged with blood early in the case. Unless this is specifically inquired for it would not be mentioned; hence hemorrhage may have been commoner than this table indicates.)	
7. Abdominal tenderness	40
8. Liver definitely enlarged in.....	20
9. Spleen palpably enlarged in.....	1
10. Pains in the back and limbs.....	36

(3) Quart. Jour. Med., October, 1916-January, 1917.

11. Urine—	
Bile	58
Albumin	33
Casts	10
12. Stools. Slate grey.....	9
13. Red blood cell count (average).....	4½ millions
14. Hemoglobin, average percentage.....	90 per cent.
15. White blood cell count (over 10,000).....	20
16. Secondary rise of fever—	
Well-marked	13
Slight	8

The pathology of this condition is discussed on the basis of autopsy in four cases. The mucous membrane of the duodenum was found to be edematous and congested; its color was dark blue, resembling a blue plum. In the first and second portions of the duodenum, small yellow patches, varying in size from pinheads to split peas, were seen through the mucous membrane—Brunner's glands (Plate VI). Round the orifice of the bile-duct there was an area about the size of a florin (approximately about the size of a half dollar), which was slightly raised above the surrounding mucous membrane; and in the center of this area was the ampulla, swollen and congested. On squeezing the gall-bladder a drop of tenacious bile appeared at the biliary orifice. The above features were seen, though in lesser degree, in the stomach and first three feet of the jejunum. The rest of the intestine was of normal appearance. At the omentum and about the bile-ducts were numerous enlarged and soft lymph glands.

The changes described in the liver are: greenish tinge, cloudy swelling, firmness in texture and slight enlargement in some instances.

In three cases, liver cells appeared practically normal, and, apart from evidence of biliary stasis, the only abnormal feature was the presence of collections of cells in the portal area, such as occur in many diseases.

In all the cases on which autopsies were done the spleen seemed to be of normal size and consistence. Cloudy swelling and scattered areas of cellular infiltration in the cortex, between the tubules and round the glomeruli, were the changes observed in the kidneys.

No morbid change was observed in the pancreas in any

instance. In the lungs there were numerous subpleural hemorrhages which extended for an inch into the lung tissue beneath, and similar, though smaller, hemorrhages within the right lung.

Patches of broncho-pneumonia were seen at the base of the lung.

In considering whether jaundice is a necessary feature of spirochetel disease, it is said that though depth of jaundice usually goes hand in hand with severity of infection, such parallelism does not always exist. It is common for a relapse of fever to occur without any interruption in the subsidence of the jaundice; in one case there was a relapse of fever after the jaundice had disappeared, but there was no return of the icterus. In one of the fatal cases the jaundice was fast disappearing during the last ten days of life when toxemia was steadily increasing. These considerations would lead one to think that jaundice, though perhaps a usual, is not a necessary manifestation of the spirochetel disease, just as typhoid may exist without intestinal ulceration. This view received support from the fact that in the units from which the jaundice patients have come there have been simultaneous cases of fever presenting somewhat similar earlier symptoms, but in which no icterus supervened. Complete confirmation is established by the occurrence of cases of spirochetosis without jaundice.

Concerning enteric jaundice, the authors say that this is an uncommon feature of enteric fever. In the campaign described in this article its incidence has been 1.38 per cent., whereas in the cases mentioned by Osler and Macrae it was 0.53 per cent. The twenty-six cases observed by the authors are divided into two groups: one in which the jaundice occurred early, *i. e.*, before the tenth day, and the other in which it occurred later in the disease. Of the total cases, typhoid accounts for six, paratyphoid *A* for four, and paratyphoid *B* for fourteen.

The actual cause of the jaundice that is associated with enteric fever is thought to be due to some obstruction in the biliary tree. They reach the conclusion that it is due to a duodenal inflammation which, in its turn, results from the localization of the infection in the duodenum. Many of the patients described in this paper have been

intubated and the duodenal fluid has contained numerous polynuclear cells of inflammation. On the other hand, typhoid and paratyphoid organisms have not been isolated from the duodenal contents, though the results of such a search have been positive in the hands of some continental and American observers.

In discussing catarrhal jaundice, as seen in this work, Dawson and Hume say that it has the features of an infection, either a mild blood infection which has localized in the duodenum, or less often perhaps an infective gastritis which has extended to the duodenum. It is a convenient term to describe a jaundice in which the infective agent has not been discovered. The usual symptoms are: headache, lassitude, a transitory mild fever, discomfort in the upper abdomen, anorexia and nausea, with jaundice supervening later. No doubt the same infections can exist without the jaundice.

An initial difficulty in making early a diagnosis of jaundice arises from the fact that so many infections have the same symptoms at the commencement of the illness. Given a patient who has head and body aches, chilliness, fever and vomiting, and he may have one of many infections, for example, enteric, trench fever, spirochetosis, influenza, or micrococcus tetragenous infection, among others determined or undetermined. The difficulty is less if the onset is gradual, for that would suggest enteric fever or spirochetosis. Both these diseases, however, can commence abruptly, and as regards enteric fever, the proportion of sudden onsets is increasing.

The characteristic catarrhal manifestations of influenza usually lead to an early diagnosis of this condition. Trench fever gives no distinguishing early picture. Captain Morris, during an investigation of the cardiovascular conditions in the enteric group, found that the heart-rate did not usually quicken after administration of 1/50 grain atropine, as the normal heart does. This phenomenon has been used to some extent as a diagnostic measure.

The appearance of jaundice after the tenth day is consistent with enteric fever, but not with spirochetosis.

The slowness of the pulse in proportion to the fever is a feature common to both enteric and spirochetosis.

Leukopenia can not be depended on as evidence of enteric. It is probably only present at the beginning of the illness, and is not even constant.

[With this statement the General Editor absolutely differs. He suspects the author had in mind enteric (typhoid) fever and also paratyphoid *A* and *B* fevers. The latter may not show leukopenia, it is true; but in typhoid fever, as it is seen in the United States, leukopenia is the most constant laboratory finding. Again and again the taking of the white blood count establishes the preliminary diagnosis of typhoid fever when other possibilities had been uppermost in the internist's mind. —GEN. ED.]

Herpes labialis is evidence in favor of spirochetosis, in which, however, it is not always present. The presence of herpes or hemorrhage in an early stage of any fever would suggest the injection of 5 c.c. of the patient's blood into a guinea-pig, even if jaundice had not appeared, bearing in mind that spirochetosis exists without jaundice, though how often is not as yet known. The finding of spirochetes in the urine may be relied upon, though perhaps two or three examinations at intervals may be necessary.

Pathology and Etiology of the Infectious Jaundice Common at the Dardanelles, in 1915. Lieut.-Col. C. J. Martin⁴ states that in the autumn of 1915 troops at Gallipoli, and to a lesser extent in Egypt, suffered from a non-fatal form of infectious jaundice, usually without complete obstruction to the entry of bile into the intestines, and not associated with any tendency to hemorrhages. It appeared to be markedly infectious; some units had 25 per cent. of their strength affected, and many cases occurred among patients in the hospital for other complaints.

The onset was characterized by lassitude, loss of appetite, headache, and often suffusion of the conjunctivae. It was ushered in with a brief period of pyrexia, temperature 101°-102° F., and generally some pain in the upper abdomen. The liver became slightly enlarged,

(4) Brit. Med. Jour., April 7, 1917.

intubated and the duodenal fluid has contained polynuclear cells of inflammation. typhoid and paratyphoid organisms isolated from the duodenal contents of such a search have been possible in continental and American observations.

In discussing catarrhal jaundice Dawson and Hume say that the infection, either a mild bacterial or viral, is localized in the duodenum, or in the gastritis which has extensive extension. A convenient term to apply to this infective agent has not yet been suggested. The symptoms are: low fever, discomfort, nausea, with jaundice in the same infection.

An initial epidemic of jaundice at Gallipoli, which have the same cause as the illness. It is due to the conclusion that the infection is spread from the duodenum to the alimentary tract. Many authorities, however, that the picture presented by the infectious jaundice at Gallipoli, and the infective hepatitis, anatomy, meager as it is, are more consistent with the view that we are dealing with hepatitis following a systematic infection than with that of a catarrhal jaundice from plugging of the bile-ducts and an extension of an inflammatory process from the duodenum. The reasons which influence him in arriving at this conclusion are stated as follows:

The illness is ushered in by a febrile attack like influenza, but usually of a shorter duration.

Jaundice does not occur for some days, and is preceded by swelling and tenderness of the liver.

Bile is rarely completely prevented from entering the intestine.

The spleen is often enlarged.

Albuminuria is not uncommon.

Notwithstanding the comparatively slight initial illness, the existence of a serious toxemia is indicated by

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Renal contents removed confirmation for the view that a bacterial infection spreading

Two patients who succumbed during the stage of jaundice showed microscopic evidence of hepatitis with necrosis of liver cells.

points out that the infectious jaundice of Gallipoli, although much milder, presents analogies to the severer form of *spirochaetosis ictero-hemorrhagica*, and contends that the symptomatology and morbid histology are consistent with the view that it is primarily a systemic infection.

Observations on One Hundred Cases of Infective Jaundice. In this article A. Stokes, J. A. Ryle and W. H. Tyler⁵ present their experiences and observations of 100 cases, fifty of which were under the personal care of one of the authors. In twenty-six of these cases the authors infected animals from the blood of patients; the animals died or were killed and the characteristic features of the disease were present. They were able to find the spirochetes in all of the animals, either in films or sections of the tissues. Early in their observations they were struck by the occurrence of cases showing a similar clinical picture, but no jaundice, and they have since been able to establish the fact that cases of spirochetosis occur without external signs of jaundice, which would seem to cast a doubt on the accuracy of the terms "epi-jaundice" and "*spirochaetosis ictero-hemorrhag-*

could be felt below the ribs and was tender to the touch; the spleen was sometimes enlarged, but not tender. Although the temperature may have returned to normal, these symptoms continued for from three to five days, when jaundice occurred and lasted for from one to two weeks or longer. The urine was bile-stained and the pulse often slow while jaundice was present.

By the time that jaundice was developed the patient generally felt better, but weakness continued, with rapid pulse and breathlessness on the least exertion. From seven to ten days after the onset of the disease a distinct increase in the area of cardiac dullness could be made out. Slight albuminuria was not uncommon. Convalescence was slow and the patient was not good for much for a month or longer.

The work of numerous authors on the subject of jaundice is quoted: It is said that Willcox and Hurst are inclined to believe that the epidemic jaundice of campaigns starts as a gastro-intestinal infection, and that cholangitis follows, due to spread from the duodenum. This view leads them to the conclusion that the infection is conveyed by the alimentary tract.

It is Martin's opinion, however, that the picture presented by the infectious jaundice at Gallipoli, and the morbid anatomy, meager as it is, are more consistent with the view that we are dealing with hepatitis following a systematic infection than with that of a catarrhal jaundice from plugging of the bile-ducts and an extension of an inflammatory process from the duodenum. The reasons which influence him in arriving at this conclusion are stated as follows:

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Notwithstanding the comparatively slight initial illness, the existence of a serious toxemia is indicated by

lassitude, which endures for some weeks, and evidence of myocardial poisoning.

Histologic evidence of necrosis of liver cells and inflammation around the portal areas is present.

Martin says, further, that no parasites were discovered in blood films taken during the disease. Blood cultures were sterile unless the jaundice supervened during an attack of typhoid or paratyphoid.

The observations made at No. 3 Australian General Hospital at Mudros do not support the conclusion of MM. Sarraillhe and Clunet at Cape Helles that jaundice was merely a manifestation of paratyphoid fever.

Bacteriologic analysis of duodenal contents removed from patients affords no justification for the view that the jaundice was due to a bacterial infection spreading up the bile-ducts.

The livers of two patients who succumbed during the convalescent stage of jaundice showed microscopic evidence of hepatitis with necrosis of liver cells.

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(5) Lancet, Jan. 27, 1917.

ica." They state that it can not be said definitely how many cases of Weil's disease occur without jaundice as a clinical sign, but they estimate that it did not occur in more than 60 per cent. of the cases of the epidemic with which they were dealing.

In describing the clinical picture of the disease, they state that the onset is marked almost invariably by a shivering fit or a feeling of faintness or giddiness. Characteristic early symptoms that have been observed were vomiting, headache, and pains in the back and limbs, pain in the eyes, and a temperature varying between 103° and 105° F. Herpes labialis, invariably becoming hemorrhagic, occurred in 42 per cent. of cases. Vomiting in the early stages may be said to be an almost constant symptom. Extreme constipation was the rule in all of the cases. One patient died from a terminal hemorrhagic diarrhea and one other had a small trace of blood in the stools. The pulse-rate was slow in proportion to the height of the temperature. No respiratory symptom save a slight bronchitis was observed early in the disease. Later, however, in 26 per cent. of the cases there was blood-tinged expectoration. Both *bright red* and *rusty* sputa were noted, the latter being the more common.

Albuminuria was almost a constant accompaniment of the pyrexial period and varied from a "faint trace" to a considerable amount. Granular tube casts and red blood cells were present in centrifugalized specimens.

Weakness and great prostration were characteristic of the disease. There was a slight enlargement of the lymphatic glands throughout the body. Varying degrees of jaundice were seen. Of forty-seven cases diagnosed as Weil's disease clinically or by communication of the disease to the animal, 74 per cent. developed jaundice, and 26 per cent. did not show any coloration. Profuse urticaria was observed in one instance. There was an irregular pyrexia descending by lysis, and ranging for the first week between 100° and 103° F., although a temperature of 104° F. was common at the onset.

Concerning the differential diagnosis of this disease, the authors say that there is seldom any difficulty in distinguishing between this and other forms of jaundice.

The high pyrexia, prostration, and conjunctival congestion, on the one hand, and the absence of any localizing symptoms on the other, exclude catarrhal jaundice, gallstones, and cholecystitis. Jaundice due to typhoid or paratyphoid infections is to some extent excluded by blood culture, which is usually done on admission. In the early stages, however, before the appearance of the jaundice and in the non-icteric cases the diagnosis is more difficult. The combination of pyrexia, herpes, and hemoptysis has not infrequently resulted in the patient being sent to hospital with the diagnosis of pneumonia, while others have been labeled pulmonary tuberculosis, suspected cerebrospinal meningitis, and "trench fever." Between severe forms of "trench fever" and non-icteric spirochetosis it is almost impossible to distinguish during the first few days unless the presence of vomiting and albuminuria in the latter and their absence in the former should prove constant.

The prognosis according to the observations of these authors has shown less than 6 per cent. mortality. The treatment has been purely symptomatic. Good nursing, unlimited fluids, alkaline drink, fruit to eat, and the rectal administration of glucose (6-per cent. solution, 1 pint) once or twice daily in cases with vomiting and acetonuria, constituted the main elements of treatment in the series. When possible the patients were nursed in the open air with apparent benefit.

The authors state that up to the time that this article was written there had been no ward or laboratory infections. The patients have been cared for in a general ward with no further precautions than would be carried out if they were enteric cases.

They believe that the clinical and experimental examination of about 100 cases of Weil's disease which they have been in a position to investigate during the last six months justifies the conclusion that the disease, as it has been observed among British troops in Flanders, is identical with that described by Inada and his collaborators in Japan.

The virulence of the infection in the cases seen in this instance was much less than that described in Japan, which is well shown by the comparatively low mortality.

All the essential findings of the Japanese authors have been confirmed, save that the culture attempts of the British camps have failed so far.

In addition to this these authors have noted the occurrence of cases of spirochetosis which did not show any external jaundice. In a footnote to this article the authors state that they have been able to confirm the statement of the Japanese workers, in regard to the finding of the spirochetes in the kidneys of the field-rats. Of nine rats taken from certain parts of a field in Flanders, five proved infective to guinea-pigs. Of six rats from other parts, one communicated the disease.

The Mild Forms of Spirochetal Jaundice. Garnier and Reilly⁶ show that spirochetal jaundice comprises not only cases of infectious jaundice with febrile manifestations, but also benign cases following the clinical type of catarrhal jaundice. In the latter, the urine contains the parasite and is able to transmit the disease to guinea-pigs. But the serum of such patients will not always protect the guinea-pig against virulent inoculations, contrary to what happens in the severe forms. However, it sometimes happens that the serum from patients with the light form will protect against the severe infection, and such were two observations reported in this work. During epidemics of jaundice, cases of catarrhal jaundice are found side by side with cases of the infectious type with remittent fever; and all have the same spirochetal origin. The blood study of all cases, slight or severe, shows similar modifications. Besides, it has been recognized for a long time that catarrhal jaundice often leaves the patient lean and anemic. In all its forms spirochetal jaundice behaves in the same fashion: A pre-icteric period, characterized by general phenomena all the way from continued fever to typhoid state or simple malaise with weakness; an icteric period, with more or less prolonged and intense jaundice, and almost constant albuminuria; finally, a tardy convalescence and slow restoration to health.

Epidemic Jaundice Among the Italian Troops. C. Moreschi and U. Carpi⁷ report that cases of jaundice

(6) *Presse méd.*, Jan. 19, 1917.

(7) *Policlinico*, Oct. 22, 1916.

were observed from the beginning of the Isonzo campaign, and that the number of cases and the gravity of the disease have steadily increased. In their cases, the disease was always well-advanced when the men reached the base hospital. In some cases the onset was insidious, the jaundice being the first symptom to attract attention; in others, there was a prodromal period with malaise, chills, and fever. Other early symptoms were sense of oppression in the epigastrium, congestion of the conjunctiva, herpes and exipistaxis. The temperature reached its highest point in the first two days and then gradually declined. In some cases the fever did not last beyond the first twenty-four hours. The intensity of the jaundice was out of proportion to the severity of the disease; in some cases it was transient while in others it persisted for weeks or months. The glands in the groin or axilla and the epitrochlear glands were often enlarged but smooth.

Of twelve guinea-pigs inoculated with about 1 c.c. of blood from the vein of three patients with this epidemic jaundice, two developed jaundice on the tenth day, with bile-pigments and albumin in the urine. A spirochete was found in the tissues, probably the same as that described by Hübener and Reiter as responsible for infectious jaundice. Tests to determine the presence of paratyphoid bacilli were almost constantly negative.

A Case of Acholuric Jaundice. The first diagnosis in this case, reported by W. H. McKinstry,⁸ was splenomedullary leukemia, but this was disproved by examination of a blood film which showed marked microcytosis and anisocytosis. These two characteristics were so striking at the preliminary examination made when first seen as to at once call attention to the urine and conjunctivae. Polychromasia, poikilocytosis, and punctate basophilia were also present, together with a few microblasts. No myelocytes were found.

Total count—

Red blood corpuscles.....5,600,000 per c. mm.

White blood corpuscles..... 5,000 "

Differential count—

Polymorphs 65 per cent.

(8) Brit. Med. Jour., July 21, 1917.

Large lymphocytes.....	20	"
Small lymphocytes	8	"
Hyalines	6	"
Basophils.....		
Hemoglobin	65	"

The blood serum was decidedly yellow, and gave an indefinite reaction for bile with strong fuming nitric acid. The serum was not hemolytic to the red cells of another patient.

The fragility of the red cells was tested with different strengths of salt solution, and at the same time controlled by blood taken from the laboratory orderly. The result is appended:

Saline Solution.	Patient's Blood.	Orderly's Blood.
1 per cent.....	No hemolysis	No hemolysis.
0.9 per cent.....	Partial hemolysis	No hemolysis.
0.8 per cent.....	Total hemolysis	No hemolysis.
0.7 per cent.....	Total hemolysis	No hemolysis.
0.6 per cent.....	Total hemolysis	No hemolysis.
0.5, 0.4, and 0.3 per cent.	Total hemolysis	No hemolysis.
0.2 per cent.....	Total hemolysis	Slight hemolysis.
0.1 per cent.....	Total hemolysis	Total hemolysis.

The man's previous history was interesting. He stated that as long as he could remember the whites of his eyes have occasionally been yellow. Almost ever since he joined the army he noticed shortness of breath, palpitation and pain over the heart on exertion, and stitch in the side. These symptoms were slight, and he paid no attention to them. Fourteen weeks before this examination, during an inspection in France, the medical officer noticed that he was "jaundiced," and he was sent to hospital, where he has remained. He had never reported sick, and complained of nothing when seen by McKinstry. He stated that he was much yellower some days than others, and that it was only discovered seven weeks previously that his spleen was enlarged.

He was ill when 8 years old with "abdominal trouble and jaundice." Since then he has been very healthy. He had never been abroad except to France (one week).

No other member of his family has ever suffered from jaundice.

Examination showed the patient to be a healthy, well-made boy, 22 years of age; skin lemon tint; conjunctivae yellow with distinct jaundice, especially around the periphery. No pyrexia; tongue, clean; digestion and appetite good. No hematemesis or bleeding from the gums.

Heart and chest, normal; pulse 80; slight pulsation of carotids and subclavians.

Abdomen: Liver felt two inches below the costal margin; edge palpable, but not hard. Spleen very large, hard, and firm. Dullness on left side of chest behind from the eighth rib downwards in the scapular line, and continuous with the splenic dullness.

There is slight enlargement of glands in the groin, but no other glands appear to be enlarged. Teeth very good, no foci of suppuration discovered; no digestive troubles; no stigmata of congenital syphilis. There is a definite jaundice tint on the soft palate.

The patient's mother supplied the following interesting facts:

"Between the age of 3 and 4 years my son (the patient) had a very bad attack of jaundice, which lasted for three weeks or longer, and for which he was attended by a medical man. Not being satisfied with the doctor attending, another doctor was called in and he found him to be suffering from a growth on the spleen. He was taken to the local hospital and detained five months. He came out of hospital in fairly good health, but two years after he had another attack of jaundice, and has had it on and off ever since. I have another son, aged 13 years, who is also yellow. I have also a little girl, aged 11 years, who is delicate and bloodless. I have had one miscarriage, and my husband is now in hospital suffering from blood poisoning resulting from ulcerated legs. This is the fourth time he has been in hospital for this disease."

From this history and from the weak positive Wassermann return of the patient's serum, McKinstry thinks that there was a strong syphilitic taint in this case.

The urine was examined on several occasions; it was at no time high colored, nor could any bile be detected chemically. When examined by the spectroscope, the

characteristic absorption band of urobilin was seen at the junction of the green and blue.

Feces were dark brown in color and free from blood.

Clinically acholuric jaundice may feature hypertrophic biliary cirrhosis, splenic anemia, Banti's disease, Addison's disease, or congenital syphilis with enlargement of the spleen and liver, but the characteristic blood changes of the former are said to be sufficiently definite to differentiate them. In making a diagnosis it is well to keep in mind one or two points—namely:

1. The blood serum of the above-mentioned diseases may contain bile.

2. Marked enlargement of the liver has been noted in cases of acholuric jaundice. In most cases, however, very little permanent enlargement is found.

3. The urine, although usually free from bile in acholuric jaundice, is on certain occasions, particularly when the jaundice is more pronounced than usual, distinctly blue-colored.

Nowadays there is a tendency among clinicians to divide cases of acholuric jaundice into familial and acquired, and in the latter group syphilis appears to be a potent factor. Whether it produces the characteristic blood and visceral changes (and McKinstry sees no reason why it should not) or whether it acts like any other debilitating agent and simply predisposes the patient to the action of other toxin or toxins is at present undetermined.

Whatever the cause of the disease may be, it appears as if some toxin acting on the spleen causes destruction of the red blood cells, with the liberation of hemoglobin, from which the liver, by increased activity, elaborates bile pigment, usually in sufficient amount to stain the skin and conjunctivae, but as a rule, not enough for it to gain access to the urine; while the bone-marrow is stimulated to increased production of red blood cells, which, owing to the demands made by the system, arrive in the circulation ill-formed and immature.

DISEASES OF THE PANCREAS.

Experimental Pancreatitis. A study of the changes in the blood-serum and the cause of death in animals in which experimental pancreatitis has been produced, has been made by William Petersen, James W. Jobling and A. A. Eggstein.¹

After a reference to the various authors who have worked upon this subject, they say that most workers are convinced that an activation (probably intracellular) of the tryptic pro-enzyme occurs with a resulting intoxication of the animal because of the sudden formation and absorption of toxic split products. Coincident with this change there may occur saponification of fats due to the simultaneous activation of the pancreatic lipase with a further injury to the pancreatic tissue by the soaps so formed. The means of activation of these ferments, resulting from a primary injury, may, of course, be diverse: bacterial infection, either to the ducts or lymphatics; mechanical blocking of the ducts and activation from bile; or activation from enterokinase and from tissue juice resulting from direct trauma, possibly from injury following vascular changes. While, therefore, the primary factor may be diverse, the resulting pathologic lesions and the cause of death are uniform.

The experiments carried out by these authors consisted of injecting bile-salts, active trypsin solution, and sodium oleate solutions into the pancreatic duct of different animals, and ligating the duct after the injection. A detailed account of three experiments is given as representative of the work done on the entire series. Results obtained are presented in tabulated form. The authors believe that they are justified in assuming that death is due to the sudden flooding of the blood-stream with the higher split products formed at the expense of the pancreatic tissue, of which the proteose-increase is an index. Except in the experiments where active trypsin is used for injection there is no increase in serum proteose at any time, as would be expected if the intoxication were a true trypsin shock, nor is there much change in serum lipase (esterase), the condition in this respect resembling

(1) Jour. Exp. Med., April, 1916.

closely the results observed following the injection of protein split products.

The increase of antiferment seems to be of distinct value in the protection of the animal; in the experiment in which soap was used for the injection this was very apparent. The increase in antiferment here was marked, while the delay in the digestion of pancreas and the consequent lessening of the shock is indicated by the gradual and relatively small increase in the amount of proteoses present in the serum. It is said, that in view of Whipple's results concerning the non-toxicity of the abdominal exudate and of the authors' experiments it would seem that the only beneficial effects which might possibly have accrued from operative interference in cases of human pancreatitis have resulted from the prolonged anesthesia rather than from the surgical drainage. The inhibitory effect of anesthetics on the development of toxicity from protein intoxication is well known. The conclusions given are:

Serum changes observed during acute experimental pancreatitis indicate that the shock and death are due to an intoxication from protein split products, and not to an intoxication from pure tryptic ferment.

When the pancreatitis is produced by the injection of an antiproteolytic substance, such as sodium oleate, the degree of intoxication bears no relation to the degree of tissue destruction.

The increase in serum antiferment apparently favors the recovery of the animal.

Functional Tests of the Pancreas. The subject of this article is "The Quantitative Determination of Amylase in Blood-Serum and Urine as an Aid to Diagnosis." It is presented in the form of a thesis by Percy Stocks,² from the Cancer Research Laboratory, Manchester. At first it was thought that all the ferments of the pancreas would be tested for, but owing to the great difficulty of finding an accurate method for determining trypsin and lipase the final work was based almost entirely upon the determinations of amylase in the blood-serum and in urine. The methods of various workers are referred to and the full detail of the one

(2) Quart. Jour. Med., April, 1916.

used, that of Wohlgemuth, is given, along with certain alterations that were made by the author. The method consisted, briefly, of adding varying amounts of urine or serum to a constant volume of standard, 1 to 1,000, solution of soluble starch, determining the amount of urine or serum that was necessary for the complete digestion of the starch, and calculating from this the units of amylase present.

A sufficient number of determinations on normals were made to demonstrate that accurate and constant results were obtained with the method decided upon. Then a study of patients with acute pancreatitis, cyst of the pancreas, nephritis, melanotic sarcomatosis, diabetes melitus, carcinoma of the pancreas, diseases of the liver and gall-bladder, and other conditions was made.

The method is described as follows: The substratum used consisted of a 1 per 1,000 solution of soluble starch, the starch being Kahlbaum's special "*Lösliche Stärke*." The exact amount of this (0.5 gm.) was weighed out accurately and distilled water added. The suspension was boiled for from eight to ten minutes with continuous stirring, by which time the fluid had become perfectly clear. The solution was then allowed to cool, made up to 500 c.c. with distilled water, and transferred to a well-stoppered bottle, a layer of toluol being poured on to prevent entrance of organisms. The bottle was kept immersed in a bucket of ice-cold water, and could be kept in this way for a long time without any change; for safety, however, a fresh solution was prepared weekly.

When a urine was to be examined, the first specimen passed in the morning was taken.

This was pipetted into a series of test-tubes, in decreasing quantities, thus:

Tubes..	1	2	3	4	5	6	7	8	9	10	11	12
Urine..	0.5	0.4	0.3	0.25	0.2	0.15	0.1	0.07	0.05	0.04	0.03	0.02 c.c.

Into each tube 2 c.c. of the starch solution were then rapidly pipetted; the tubes were inverted to ensure mixing, and at once transferred to a beaker of water at 40° C., which, after bringing to approximately 38° C., was placed in an incubator at this temperature.

This was done because an air incubator raises the fluid

in the tubes only slowly to its own temperature, so that this is better done by a water-bath which is adjusted to the right temperature and quickly transferred to the air incubator. This is important when working with a short digestive period, as here.

At the end of thirty minutes the tubes were removed from the bath and plunged into cold water to arrest digestion. A few drops of N/50 iodine solution being now added to each tube a beautiful gradation of color is produced. In the tubes where starch is still undigested the color is deep blue, where digestion is complete this is yellow, and in the intermediate ones violet and red, this gradation, blue—violet—red—yellow, corresponding to the change from starch to sugar by way of erythro-dextrin and achroödextrin.

The tubes which show no blue color at all are those in which no starch remains, and the lowest of these next to the first purple one is taken as the limit ("Limes")—that is to say, it contains just enough amylolytic ferment to change 2 c.c. of 1/1,000 starch solution.

Reduction to units is done as follows:

α = number of c.c. of urine required to digest 2 c.c. of starch solution (1:1,000) in 30 minutes at 38° C.

D 38°, 30" = number of amylolytic units per c.c. of urine, determined under these conditions. .

$$D\ 38^\circ, 30'' = \frac{2}{\alpha}$$

e. g., supposing the last tube in the series which contains no blue tint to be No. 6, then

$$\alpha = 0.15 \text{ c.c.},$$

$$D\ 38^\circ, 30'' = \frac{2}{0.15} = 13.3 \text{ units.}$$

In case of blood-serum, this is obtained by puncture of the antecubital vein with a cannula, the blood being then centrifuged and the serum decanted off. The process of examination is the same as for the urine, the amounts of serum added to the tubes of the series being for convenience:

Tubes..	1	2	3	4	5	6	7	8	9	10	11	12
Blood..	0.5	0.4	0.35	0.3	0.25	0.2	0.15	0.12	0.1	0.07	0.05	0.04 c.c.

Exactly the same procedure is followed as for the urine, and the value of D per c.c. of serum is calculated as before.

To meet the variation possible from differences in concentration the factor D determined from the single specimen was multiplied by the number of c.c. in the twenty-four-hour specimen. This was found to give practically a constant, representing the secretion of amylase for the day, and is designated as M.

Practically all the body fluids were tested for amylase, with the result that it was found to some degree in each of them.

The value of D, calculated from the amylase in urine of normal individuals, was found to be from 10 to 13.3 units per cm.; for normal serum it was from 6.6 to 8 units. In the various disease conditions studied the factors were found to vary greatly, D for urine being as high as 100 in carcinoma of the pancreas, and 66 in conditions causing passive congestion of the pancreas.

The conclusions arrived at from this work are:

Amylolytic ferment is present in the blood-serum and urine of all healthy individuals, and has also been found in the body fluids examined.

The level is practically constant in the blood-serum—the level in the urine is subject to diurnal variations due chiefly to the digestive functions.

The ferment is of pancreatic origin and is absorbed directly by the blood.

No proof of the action of anti-amylase has been found.

Disease of the kidneys causing any diminished permeability of these organs reduces the amount of ferment in the urine and consequently raises the amount in the blood.

Any disturbance in the ratio D (blood) : D and M (urine) indicates renal insufficiency in all such cases.

Severe passive congestion also raises the amount of amylase in the blood.

With these exceptions any increase of the ferment in the blood-serum denotes pancreatic mischief.

The values have been found raised in all cases of pancreatic disease, the increase depending on the degree

of obstruction in any part of the gland or its ducts, and on the acuteness of the condition.

The highest values were found in a case of acute pancreatitis.

The estimation of the amylolytic capacity of the blood-serum and the urine is a most delicate test of the efficiency of the pancreas, and consequently is a most delicate and reliable test for disease of the pancreas.

The use of the simplified modification of Wohlgemuth's method, and the use of an identical technique for serum and urine, are justified by the consistency and regularity of the results obtained.

Acute and Sub-Acute Pancreatitis. This article by Stephen H. Watts,³ of the Medical School of the University of Virginia, is based upon the literature of the subject and the records of seven patients treated in the author's own practice.

According to the literature, this disease occurs about twice as often in men as in women, but in the author's seven cases there were five women and two men. The disease usually occurs between the ages of 20 and 50. Obesity and alcoholism are believed to favor its occurrence. The presence of disease of the gall-bladder and bile-ducts in a high percentage of patients suffering with pancreatitis has been noted by many writers. Especially is this true if a gall-stone has passed through the ampulla of Vater and occludes the pancreatic as well as the bile-duct. In such conditions bile, and in many instances, infected bile is thrown directly into the pancreatic duct. It has been shown experimentally that bile alone in the pancreatic duct is sufficient to produce an acute pancreatitis. It is said that the physiologic investigations of Pavlov and his pupils have shown that under normal conditions the pancreatic juice is inactive but is activated by enterokinase, by which trypsinogen is changed to trypsin. When this occurs within the gland, digestion takes place and the enzymes are liberated into the gland and surrounding tissues, extensive necrosis resulting. Among other substances in the body which seem to be able to activate the pancreatic juice are the duodenal contents, bacteria, blood-serum, and bile, especially when

(3) *Memphis Med. Month.*, October, 1916.

the bile is infected. Particular attention has been called to the important part played by bacteria in activating the pancreatic juice in cases of acute pancreatitis.

The presence of pancreatic stones has also been shown to be the cause of acute pancreatitis in certain instances. By some it is thought that next to gall-stones gastrointestinal disorders are the most common etiologic factors. The effect of a gastro-duodenitis producing an occlusion of bile into the pancreas has been considered an important factor. Other causes mentioned in the etiology of this disease are typhoid fever, mumps, trauma, gastric ulcer, appendicitis and syphilis. The organism most commonly present in acute pancreatitis is *Bacillus coli communis* and next in frequency streptococci and staphylococci. Infection passes directly from the bile-ducts, directly from the intestine into the pancreatic ducts and sometimes by the blood-vessels and lymphatics, or directly through the intestinal wall into the pancreas itself.

The pathologic picture presented by this disease is a greatly swollen gland, usually of softer consistency than normal, especially when the hemorrhagic infiltration and necrosis are extensive. It presents a dark reddish, mottled appearance, and on microscopic examination there are areas of necrosis which stain poorly with the aniline dyes. About these necrotic areas there is a zone of inflammation and scattered through the involved gland there are more or less extensive areas of hemorrhagic infiltration. Sometimes the whole pancreas seems to be nothing but a mass of necrotic tissue.

It has been determined that the small yellowish spots seen in the tissues of the abdomen in this condition are due to the presence of the fat-splitting ferment, steapsin, which produces areas of saponification, neutral fat being split into glycerine and fatty acid and the latter combining with calcium in the tissues to form soap. One of the most striking symptoms of the disorder is acute, agonizing pain in the epigastrium, which is so extreme that it may rapidly bring on collapse and may actually cause syncope. Vomiting soon occurs and may lead to the mistaken diagnosis of intestinal obstruction. Constipation is almost absolute and distention of the abdo-

men forms a prominent feature in the clinical picture. Tenderness and rigidity are usually present, but not extreme. The pulse becomes rapidly weak and small and the temperature varies from sub-normal to as much as 104° F.

Glycosuria occurs only late in the disease. It was found by the author in only one of his seven patients.

The usual functional tests for pancreatic functions are of but little if any value in the diagnosis of this condition.

Death usually occurs in from two to five days from collapse and is thought to be due finally to toxemia due to the absorption of the products of cell-decomposition caused by self-digestion of the pancreas.

In making a diagnosis the condition must be differentiated from intestinal obstruction, peritonitis resulting from a perforated gastric or duodenal ulcer, ruptured gall-bladder or diseased appendix. The diagnosis is often impossible and is arrived at definitely only when an exploratory laparotomy has been performed.

The treatment discussed in this article consists of prompt surgical interference as soon as the disease is suspected. Many instances have been noted by several different surgeons in which the removal of gall-stones or an infected gall-bladder have been coincident with prompt recovery from acute pancreatitis.

The treatment of sub-acute pancreatitis and pancreatic abscess consists of surgical drainage. The prognosis as indicated by the report of various groups of cases in the literature is at best very serious. The statement is made that recent statistics of operations for acute pancreatitis gives the mortality as from 50 to 60 per cent.

Acute Alcoholic Pancreatitis. Among the post-mortem examinations performed by William St. C. Symmers⁴ at Queens University, Belfast, during the last eight years, there is a remarkable series of thirty-one cases in which death was sudden. In each instance there was a distinct history of more or less habitual drinking to the extent that would be called "hard drinking"—indulged in day by day as a matter of custom. The patients were all adults and apparently vigorous and able

(4) Dublin Jour. Med. Sci., April, 1917.

to attend to their business, well-nourished, and in one case in very comfortable circumstances.

The post-mortem appearances were identical in all the cases. Brain, lung, heart, coronary arteries, kidneys were normal to the naked eye. Constant lesions were observed in the stomach and pancreas, and in no other part of the body were there any signs significant of morbid change.

In the stomach there were found more or less general catarrh and areas of stippled hyperemia which varied in shape and size from irregular ribbons half an inch broad by two inches or more in length, to more or less circular plaques two or more inches in diameter with an irregularly radiating jagged circumference.

The pancreas was distinctly redder than normal; the color was bright red, due not only to general redness of the parenchyma, but also to irregularly stellate, bright or dark red accumulations of blood at the angles between adjacent lobuli, at times appearing as small hemorrhages in these angular interlobular spaces. On section, this same inflamed appearance was marked, the parenchyma being reddened as if the gland cells were tinted by effused blood, and the interacinous spaces showed as stellate or angular areas crammed with blood. The whole naked eye aspect of the organ was that of an unduly red hemorrhagic tissue, contrasting markedly with the usual pallor of the pancreas as seen at post-mortem examination.

There was never any regurgitation of bile into the pancreas, nor were gall-stones present in any of the cases. Fat necrosis was absent.

Hemorrhagic condition of the pancreas varied in intensity, some cases showing actual hemorrhages as dark red splashes shining through the connective tissue of the organ, or even implicating most of the gland, so that most of its extent was covered by blood, but most frequently this hemorrhage was absent, the gland showing merely generalized reddening of its tissues, with interacinous over-crowding of the blood-vessels.

Microscopically the pancreas showed marked congestion of blood in the fibrous septa of the gland, and also in certain of the smaller capillaries in the substance of

the organ, at times with an effusion of red cells among the glandular acini. As a rule, the destruction of the tissue had not proceeded to a marked extent, so that the parenchyma was still recognizable as pancreatic, with cells shrunk away from the surrounding fibrillar tissue, which, therefore, imposed itself as being more abundant than normal. There were numerous isolated pancreatic cells, with no acinous arrangement, staining badly with logwood, and often taking up the eosin strongly.

The author states that in these thirty-one cases a complex of alcoholic indulgence, sudden death, gastric hyperemia of the peculiar form, and a necrotic condition of pancreas was found. At present he prefers to call this condition acute pancreatitis probably due to alcohol.

Acute Hemorrhagic Pancreatitis. W. Linder⁵ of Brooklyn reports that in three years he has seen thirty-three cases of this condition. He emphasizes the importance of keeping the possibility of hemorrhagic pancreatitis in mind when there is any acute abdominal condition. This is not necessarily a fatal disease, he says; there are more cases of the mild than of the fulminating type. If recognized early they need not become serious; but early diagnosis is imperative if good results are to be secured.

The treatment he advocates is operative. In one-third of his cases he found associated gall-bladder disease.

Pancreas Intoxication. Concerning this subject E. W. Goodpasture,⁶ of the Peter Bent Brigham Hospital and the Harvard Medical School, of Boston, states that two main views are held regarding the nature of the toxic agent of the autolyzing pancreas. One identifies it with active trypsin, the other with split products of protein resulting from trypsin digestion.

The author's study was undertaken with the idea of purifying, so far as possible, the toxic part of the autolyzing gland. It was found that fresh pancreas extract in salt solution was toxic, and when injected intravenously produced symptoms of poisoning analogous to

(5) Paper read at annual meeting of Med. Soc. State of New York, Utica, April, 1917.

(6) Jour. Exp. Med., February, 1917.

those resulting from duodenal loop fluid, and other toxic materials of a protein nature. It was decided that the preparation of fresh pancreas extract contained but little if any active trypsin. It seemed probable, therefore, that trypsin was not the active toxic agent, but some other substance present in the normal gland. Extracts of the normal gland were found to be definitely and fatally toxic to animals. Experiments carried out with this idea in view, revealed the fact that the β -nucleo-protein fraction of the gland was toxic and produced reactions identical with those following injection of the salt solution extract of the fresh gland.

Preparations from autolyzed pancreases were found to contain guanylic acid, and to determine whether this was sufficiently toxic to produce the symptoms noted or not, this acid was used alone and found to be not the toxic agent.

The author, after using these various preparations of normal and autolyzed pancreas, concludes that a toxic constituent is present in the fresh pancreas of dogs before trypsinogen can have been activated. The toxic fraction is present in the β -nucleo-protein and, therefore, is thermostable. It is gradually destroyed by autolysis but can be obtained in concentrated form from a gland which has autolyzed 24 hours. The toxic material is probably protein in nature. Intravenous or intraperitoneal injection of from 0.05 to 0.1 gm. per kilo of body weight is usually fatal and elicits in dogs symptoms comparable to those of spontaneous hemorrhagic necrosis of the pancreas.

Pancreatitis Due to Ascarides. Four cases are reported by G. Izumi.⁷ He states that search of the literature showed only one report of such a case in a human being and one in a cat.

In his cases persistent pain in the region of the pancreas necessitated removal of that organ; ascaris ova were found imbedded in a circumscribed inflammatory area. In one case a long ascaris was found in the pancreatic duct and in the tail of the pancreas. In all the cases, the stomach, liver, and biliary ducts were apparently normal.

(7) Mitt. a. d. Med., Fak., Kyushu Univ., Japan, vol. 2, p. 61.

Izumi also reports experiments on nine dogs injected with an emulsion of ascaris ova into the pancreas; controls received injections of isotonic salt solution. The findings confirm those in the clinical cases, showing that irritation from immigrated ascaris eggs is liable to set up chronic circumscribed pancreatitis. No fat tissue necrosis was found in the animals, although it was pronounced in the clinical cases. This suggested to Izumi further research on the causation of acute hemorrhagic pancreatitis, and he cites the details of experiments on ninety-six other dogs, showing the effect on the pancreas of interference with its circulation, of obstruction of the outlet, of injected duodenal content, injected olive oil, steapsin, hydrochloric acid, sterile or infected bile, blood and serum, trypsin, pancreatic juice or extract of duodenal mucosa. The data confirm the belief that the trypsinogen element of the pancreatic juice is responsible for acute hemorrhagic pancreatitis, but first it must be activated, and an extract of duodenal mucosa is the most potent activator. All other factors are of minor importance, Izumi declares, in the genesis of necrosis of the pancreas.

Tumor of Pancreas Causing Symptoms of Gallstones.

A patient was referred to G. Onano⁸ for operative removal of gallstones as the man was suffering from colic and jaundice. In palpating the liver and gall-bladder Onano noted an abnormal pulsation and sensation of friction, with a murmur very distinct on auscultation, applying the stethoscope a fingerbreadth to the right of the umbilicus. These findings were peculiar and not to be detected in other patients with gallstones or in the healthy, and suggested that the pain and jaundice might be the result of compression of the common bile-duct from some tumor, especially as there was no fever and acute inflammation could be excluded. At the same time the idea of a tumor did not harmonize with the periodical return of the colic about once a week, or with what seemed to be an enlarged gall-bladder, which could be palpated under the edge of the large lobe of the liver. Roentgenoscopic examination was negative, but this

(8) *Gaz. d. osp. ed. clin.*, July 30, 1916.

might be explained by the gallstones being formed of cholesterin. The abdomen was opened. The gall-bladder was found normal and the trouble was found to be a large tumor in the pancreas. In a similar case the compression inducing the recurring colic and jaundice was found to be due to an aneurysm of the celiac artery.

The Fate of Trypsin in the Stomach. Concerning this subject the following Editorial⁹ is instructive:

The proteolytic enzyme of the pancreatic secretion has long been regarded as exceedingly sensitive to acids. In the presence of even low concentrations of acids, the tryptic power seems to be permanently diminished or completely lost. Many believe that gastric juice is peculiarly destructive to the proteolytic pancreatic ferment by virtue of the action of pepsin on the enzyme. There is a practical aspect to this. On the one hand it concerns the possible survival of tryptic power when intestinal contents are regurgitated into the stomach, as occasionally happens. On the other hand, the futility of administering trypsin preparations by way of the mouth must be gauged in part by the fate of the enzyme in its contact with the gastric contents. Judging by experiments which Long and Hull¹⁰ have conducted *in vitro*, it appears that the common proteolytic enzyme of the pancreas, isolated as trypsin, is capable of withstanding a rather long digestion in presence of hydrochloric acid and pepsin, provided sufficient protein of some form is present to combine with all or part of the acid and so bring the hydrogen-ion concentration down to a certain level. They¹ have now corroborated these findings by a study of what happens in the living stomach of animals under conditions which might well obtain in the human stomach at times when trypsin is ingested. Long and Hull report new experiments in which the secretion of pepsin and acid was abundant, and from this point of view the conditions for the persistence of trypsin were not favorable. Yet, in the larger number of experiments, the latter ferment was not destroyed by the other combination when sufficient protein

(9) Jour. Amer. Med. Ass'n., Feb. 17, 1917.

(10) Long, J. H., and Hull, Mary: Assumed Destruction of Trypsin by Pepsin and Acid. Jour. Am. Chem. Soc., 1916, 38, 1620.

(1) *Ibid.*, 1917, 39, 162.

was present to bring the concentration of the free acid down to a certain value. Trypsin seemed to be destroyed or greatly weakened only when the acid was in excess with pepsin. From these observations it appears, further, that possibly some tryptic digestion may occur even within the stomach when the free acid is low from protein combinations; and the destruction or weakening of the trypsin is a function, probably, of the hydrogen-ion concentration. The trypsins employed in these experiments were relatively strong products. It is not to be concluded that these results even remotely suggest that the administration of a few grains of the various commercial products claimed to contain trypsin or pancreatin would have any therapeutic significance. In the dosages employed, such preparations are, as has been shown elsewhere, too weak to have any appreciable action.

Tryptic Broth as Culture Media. The preparation of a standard nutrient medium, to be used instead of peptone media, has been carried out by Sydney W. Cole and H. Onslow.² The final material and the method used for preparing it followed a considerable amount of experimental work. The description is given as follows:

Obtain the fresh pancreas of a pig, free it from fat as far as possible, and weigh. Mince it finely and add three times its weight of distilled water and its own weight of strong alcohol. Shake well in a large bottle and allow it to stand for three days at room temperature, shaking the bottle occasionally. Strain through muslin and filter through a large folded paper. The filtrate, which comes through very slowly, is measured and treated with 1 c.c. of concentrated hydrochloric acid for every liter. This causes the appearance of a cloudy precipitate which settles in a few days and can be filtered off. The fluid keeps for an indefinite period, if stoppered, without any added antiseptic. If desired at once the extract may be used before adding the hydrochloric acid, the function of which is to retard the slow auto-destruction of the trypsin.

Digestion of Casein: A material known as "Laitproto No. 6, for bacteriologic purposes," made by a firm in

(2) *Lancet*, July 1, 1916.

London, is used in this preparation. To 1 liter of tap water add 20 g. of anhydrous sodium carbonate and boil in a 2-liter flask or evaporating dish. When boiling, transfer the dish to a boiling water-bath and add gradually 200 g. of the casein. This must be "dusted" in carefully and well-stirred to avoid clumping. Transfer to a Winchester quart and wash out the mixing vessel with a liter of cold tap-water which is also transferred to the bottle. If necessary, allow the temperature to fall to 40 degrees C. and add 50 c.c. of the pancreatic extract, made as above described, and 15 c.c. of chloroform. Shake well, stopper with a loose cork, and incubate at a temperature of from 37 to 40 degrees C., shaking the bottle vigorously each day to break up any clumps. After five days' digestion, add another 50 c.c. of the pancreatic extract and allow the mixture to incubate for another ten days.

To prepare the stock broth, the warm mixture is well shaken to break up any crusts of tyrosin that may have formed, and is transferred to a large (3-liter) flask, treated with 400 c.c. of normal hydrochloric acid (or 40 c.c. of pure concentrated hydrochloric acid diluted with 360 c.c. of distilled water), shaken, steamed for thirty minutes, and filtered. The filtrate is treated with 120 c.c. of normal sodium hydroxide and the reaction adjusted.

Tryptic broth is prepared by diluting the stock broth with twice its volume of 0.5 per cent. sodium chloride dissolved in tap-water and adjusting the reaction. For the latter the following solutions and procedure are given:

A. The indicator.—0.1 g. of phenol-sulphone-phthalein is transferred to a liter measuring flask and treated with 10 c.c. of N/10 sodium hydroxide and about 500 c.c. of distilled water (previously boiled and cooled). 10 c.c. of N/10 hydrochloric acid are then added and the volume made up to 1 liter with distilled water.

B. Phosphate mixture $P_H = 7.3$.—Dissolve 9.085 g. of pure disodium-phosphate ($Na_2HPO_4 \cdot 2H_2O$) and 2.133 g. of pure monopotassium phosphate ($KH_2PO_4 \cdot 2H_2O$) in distilled water and make up the volume to 1,000 c.c. with freshly boiled distilled water. To 100 c.c. of the phosphate solution add 10 c.c. of the indicator, stopper, and keep in the dark.

C. Phosphate mixture $P_H = 7.4$.—Dissolve 9.596 g. of the di-

sodium phosphate and 1.743 g. of mono-potassium phosphate in distilled water and make up the volume to 1,000 c.c. with freshly boiled distilled water. To 100 c.c. of this phosphate solution add 10 c.c. of the indicator, stopper, and keep in the dark.

D. N/20 hydrochloric acid.—To 1,000 c.c. of N/10 hydrochloric acid (or 100 N. hydrochloric acid) add 182 c.c. of the indicator and distilled water to make the volume up to 2,000 c.c. Keep in the dark.

E. N/20 sodium hydroxide.—To 1,000 c.c. of N/10 sodium hydroxide (or 100 c.c. of N. sodium hydroxide) add 182 c.c. of the indicator and distilled water to make the volume up to 2,000 c.c. Keep in the dark.

Six tubes are placed in the holes of a box, and to them are added the following solutions: (2) and (6) some of the broth, (4) distilled water, (1) some of solution *B*, (5) some of solution *C*, (3) 5 c.c. of the broth (accurately measured), and exactly 0.5 c.c. of solution *A*. (It is essential that the broth for this tube be boiled for half a minute in a test-tube and well cooled under the tap before it is measured, because subsequent sterilization causes a change of PH). The box is then held up to the light and the tubes examined by looking through the slots *X*, *Y*, *Z*. It will then be noticed that *Z* is redder than *X*. It is necessary to adjust the reaction of the broth in 3 so that *Y* appears to be intermediate in color between *X* and *Z*. If it is redder than *Z* it must be titrated with the acid solution *D*. If it is yellower than *X* it must be titrated with the alkaline solution *E*.

For the titration microburettes are employed containing 2 c.c. graduated in 1/50 c.c. so that they can be read in 1/100 c.c. The acid or alkali is slowly added to tube 3 until its color is judged to be intermediate between the two standard tubes when they are viewed through the box. Should the titration be performed with acid solution, allowance has to be made for the change in reaction that occurs from the loss of carbon dioxide in the subsequent sterilizations. A rough method of overcoming this difficulty is to boil the contents of Tube 3 for 15 seconds, cool thoroughly, and add more acid until the reaction is again correct. This may have to be repeated more than once. Normal hydrochloric acid and normal sodium hydroxide (and tenth normal solutions of these substances if the total amount required is expressed in

TABLE SHOWING ACID AND GAS PRODUCTION ON TRYPTIC BROTH AND STANDARD PEPTONE WATER.

Organism.	Broth.	5 Hours.		7½ Hours.		8½ Hours.		10 Hours.		12 Hours.		24 Hours.		48 Hours.	
		Acid.	Gas.	Acid.	Gas.	Acid.	Gas.	Acid.	Gas.	Acid.	Gas.	Acid.	Gas.	Acid.	Gas.
<i>B. Paratyphosus A</i>	Tryptic	—	0	+	0	+	+	+	0	+	+	+	+	+	+
16.....	Standard	—	0	—	0	—	—	+	0	+	+	+	+	+	Trace
<i>B. Paratyphosus A</i>	Tryptic	—	0	+	0	+	+	+	0	+	+	+	+	+	0
17.....	Standard	—	0	—	0	—	—	+	0	+	+	+	+	+	0
<i>B. Paratyphosus A</i>	Tryptic	+	0	+	0	+	+	+	0	+	+	+	+	+	Trace
48.....	Standard	—	0	—	0	—	—	+	0	+	+	+	+	+	Trace
<i>B. Paratyphosus B</i>	Tryptic	+	0	+	0	+	+	+	1	+	+	+	+	+	Trace
Standard	—	0	0	—	0	—	—	+	0	+	+	+	+	+	Trace
<i>B. Typhus 40</i>	Tryptic	—	0	+	0	+	+	+	0	+	+	+	+	+	Trace
Standard	—	0	0	—	0	—	—	+	0	+	+	+	+	+	Trace
<i>B. Coli Communis</i>	Tryptic	+	0	+	5	+	+	+	5	+	+	+	+	+	Trace
23.....	Standard	—	0	+	3	+	+	+	5	+	+	+	+	+	Trace
<i>B. Coli Communior</i>	Tryptic	+	0	+	4	+	+	+	6	+	+	+	+	+	Trace
50.....	Standard	—	0	+	0	+	+	+	7	+	+	+	+	+	Trace

— indicates no change of reaction. + indicates faint acidity. ++ indicates marked acidity. +++ indicates full acidity. The figures indicate the amount of gas in the Durham tube, measured in millimeters —e. g., ++, 0 = marked acidity, no gas.

more than two decimal places) is then added to the bulk of the broth, depending on whether acid or alkali is used for the original titration. For every 0.1 c.c. of N/20 acid or alkali required for the titration of 5.0 c.c., 1 c.c. of normal acid or alkali is added to each liter of the tryptic broth. If special accuracy is required the bulk of the media can be restandardized after steaming. Sterilization by steaming on three consecutive days is preferable to autoclaving. The medium is then ready for distribution and use.

Some of the advantages of this media are, that it is very cheap, especially as compared with peptone; its composition is sufficiently constant to yield uniform results; the reaction is constant; on it a luxuriance of growth can be obtained that has not been approached by the use of peptone; owing to its richness in free tryptophane it is of excellent use in testing for indol formation; when diluted with its own volume of 0.5 per cent. sodium chloride solution it is an excellent medium for detecting acid and gas formation; it is particularly useful in the preparation of agar and special media, such as Endo, etc.; and lastly, there are indications that this broth will be of special use with brilliant green because of the selective restraining power of the combination on the growth of *B. coli*.

The acid and gas production on tryptic broth and standard peptone water are shown in the table on page 335.

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